as the beginning of the " unorganised " period—very
it started earlier—the patient was then 28 You
mber I asked the rhetorical question of what would
happened to the woman patient if her doctor,
ad of asking his hesitant questions, had sent her for
dotherapy Although admittedly our second patient
r more ill than the woman his case could be con
ed as a pointer of the direction the woman's illness
it have taken We may here ask the corresponding
tion of what would have been the fate of this man if,
ad of sending him to specialists and prescribing him
les and bottles of medicine, someone had asked a few
nent questions at the right moment Who knows ?
nyhow, our man settled down and created and grew
mpressive illness involving his whole life Although
superficial symptoms varied and changed, the basic
ture of the illness remained the same and became
er and firmer with the years One aspect of the
s was to play hell with his practitioner, to rub in
and again that he was no good, absolutely useless
cannot exclude altogether the possibility that this
partly a revenge for the doctor s rejection of the
nt's propositions. Although it is not mentioned in
report, we can well imagine that there were quite a
not very pleasant periods for the doctor He asked
help from his specialist colleagues, but what he got
only negative advice That is, he was told what
o do, but he got no help whatever on how he could
his atient. I wonder how many of us—whether
ral practitioners, psychologists psychiatrists or
l workers—would have remained under this irritat
re, as calm and imperturbable and as friendly and
pathetic as *our doctor How many of us would have*
ght of taking down the pharmacopœia and offering
cerely to the patient to choose from it the medicine
inks might help him

was this atmosphere of unshakable friendly sympathy
enabled the patient to make his peace with his bad
useless doctor and to accept his company for all
troubled years of illness, pain, and suffering He has
ously been badly in need of company, and without
doctor he would not have been able to keep fit and
tain a tolerable or perhaps even a not completely
ppy, private life

sum up in this case all the organic illnesses
osed by the patient were rejected one by one but
doctor accepted the pain and the suffering and
tly tried at least to relieve them. This counter
ition of his was in turn rejected by the patient,
perhaps prompted also by his resentment—wanted
ve his doctor bad and impotent The doctor then
d to this last proposition—i e , that he cannot
e the suffering and pain and agreed also to remain
lly and sympathetic On these terms a working
romise was established and patient and doctor
d down to a form of illness acceptable to them both

* * *

w imagine that this patient had been on the list
doctor who—because of his personality—must be
od and helpful man whose apostolic function
els him to try everything in his power to cure his
nts without exception—or mercy

* * *

romised to talk about The Doctor, His Patient and
Illness But really ' the doctor " should have been
plural, for in any difficult case specialists are called
advise This brings in quite a number of new
lications. From now on the patient cannot escape
g that he has got to deal with the whole medical
ssion facing him a single person in concerted
n. This inevitably stirs up reminiscences of his
life, when, as a single child, he had to face the whole
of adults who tried to educate him in their
tolic function It is in this way that the present
situation mobilises all the anxieties animosities, fears and frustrations blind confidence and dire suspicions, of that early age This fact explains why so many patients regress to surprisingly childish methods in their relation to their doctor or doctors—e g to complete subordination, or swearing blindly by the doctor s words , to an almost crazy rebelliousness ridiculing and belittling anything and everything that the doctor proposes , or to a habit of playing off one doctor against the other But behind their unrealistic attitude is always the gnawing fear and the abject dependence They feel that possibly something very important has gone wrong in their body or mind that they cannot put it right by themselves , but that almost certainly this can be done by outside expert help With this help they may survive ; without it they are doomed

* * *

We know that during the initial unorganised " period of their illnesses, patients gradually withdraw from their environment and first create and then grow the illness on their own, out of themselves This period is only poorly understood our psycho analytic methods do not enable us to follow in detail the patient in his struggle with the growing illness In this situation there is as yet no second powerful person present, and certainly no external partner on whom emotions could be transferred and thereby made accessible to our analytic methods But the situation changes fundamentally when the patient reaches the stage of complaining Although his illness is usually still unorganised he now needs, and usually also finds, a partner a superior one, from whom help can be expected on whom emotions can be transferred. Here we analysts are more at home and can use our methods with more confidence, and our ideas may be of some use to the general practitioner in his arduous task

It is equally true however, that we can also learn from the experiences of the general practitioners , for it is only seldom that we see patients in the unorganised state in which the practitioner first encounters them, and we have mostly avoided getting involved with them at this stage On the other hand the psycho analytic process is tantamount to stirring up rigid, settled in attitudes and forms of reaction, and almost every day we witness and have to work with both kinds of transition —from organised to unorganised and from unorganised to organised states Expressed in our new terms we find again the patient proposing something to his analyst and the analyst responding to it according to his own apostolic function Compared with the general practitioner we analysts are in a better position because we possess a considerable literature which advises us in some detail which parts and aspects of the material produced by our patient should be interpreted when and how Despite this important difference the apostolic function operates automatically—exactly as in the case of the general practitioner The illness as it develops and changes in the two person analytic situation is always the result of a compromise, of an interaction between the analyst and his patient

To show what I mean by this interaction I wish to quote a historical example

In Freud's early writings the illnesses most frequently mentioned were hysteria, phobia, and the group he called actual neuroses foremost amongst them neurasthenia. It was he who detached from that group the obsessions, and in the next period these seem to have dominated the field. In still later years actual neuroses practically disappeared from the literature and almost every case was described either as character neurosis or neurotic character disorder Nowadays we have learnt to recognise the importance of depressive paranoid and other psychotic mechanisms in nearly all our cases

Does this mean that the patient material itself has changed ? In my opinion it means rather that our knowledge of the human mind has changed, has deepened

6244

and widened, and that consequently our responses to the patient's propositions and offers are different now from what they were fifty, thirty, or even twenty years ago A consequence, and a very important one, of this change in our responses, in our apostolic function, is that by them we determine, so to speak, the main spheres of the mind, where the most important parts of the analytic work have to be done This may explain why analyses today are so different from what they used to be

I have discussed the need for the general practitioner to respond to his patient's propositions in such a way that the ensuing compromise should focus attention and interest on the proposition which offers the best prospect of therapeutic help But there is equal need for us psycho-analysts to ask ourselves whether our present responses to our patients' propositions—i e our present ways of interpreting the material produced by the patient—lead to a compromise which focuses attention, interest, and libido on the proposition which offers the best prospect of therapeutic help

I know that these ideas throw a heavy and alarming responsibility on all of us—general practitioners, specialists, psycho-analysts alike—but I cannot see how any one of us can avoid shouldering it And I firmly believe that by becoming more and more aware of our roles in the patient-doctor relationship—i e , of our side effects as drugs—our therapeutic efficiency will grow apace

POSTSCRIPT

Throughout this address I have used the word "illness" in the same sense as it is used in general medicine For example, in the first case discussed, the four conditions were described as illnesses in their own right, although obviously they may influence one another or one may be secondary to the other

If I am right, psycho-analysis is about to develop a new conception, which may be called "basic illness" or perhaps "basic fault" in the biological structure of the individual, involving in varying degrees both his mind and his body The origin of this basic fault may be traced back to a discrepancy in the early formative years (or possibly months) of the individual between his own needs and the care and nursing available at the relevant times This creates a state of deficiency whose consequences are only partly reversible Although the individual may achieve a good, or even very good, *adjustment* the vestiges of his early experiences remain and contribute to what is called his constitution his individuality, or his character make-up both in the psychological and the biological sense The cause of this early discrepancy may be congenital—i e , the infant's needs may be too exacting—or may be environmental, such as insufficient careless, haphazard, over-anxious, over protecting, or only un-understanding care

Should this theoretical approach prove correct, then all the pathological states of later years the "clinical illnesses," must be considered as symptoms or exacerbations of the "basic illness," brought about by the various crises in the development external and internal, psychological or biological of the individual I wish to explain that my address was concerned only with the "clinical illnesses" of later years and not at all with the "basic illness"

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how far can the general practitioner be rigidly scientific and if he could and did would he not become the 'medical technician' of whom some doctors disapprove? Who would then deal with the patients disabilities, inabilities, disorders, as distinct from narrowly defined 'diseases'? And would the patient, *qua* patient, be allowed to be neurotic, or ever normally worried or subject to conflicts? Would the average doctor be happy if his 'non scientific' problems were handed over entirely to almoners, social workers, psychiatric social workers, marriage guidance counsellors, family welfare advisers poor man's lawyers and specially selected priests? Most of these perform their functions excellently when properly chosen and trained but would the increase in their responsibilities and numbers decrease those of the doctors as we understand the term?"—T H PEAR *So[illegible] in English Life* London, 1955, p 39

BILATERAL LUMBAR PLEXUS LESIONS SIMULATING CAUDA-EQUINA COMPRESSION

ALEXANDER R TAYLOR
M A , M B Aberd , F R C S E
NEUROLOGICAL SURGEON, ROYAL VICTORIA HOSPITAL, BELFAST

NORMAN M DOTT
C B E , M B Edin , F R C S E , F R S E.
PROFESSOR OF NEUROLOGICAL SURGERY, UNIVERSITY OF EDINBURGH

INFLAMMATORY disease of vertebral bodies, commonl tuberculous, often proceeds to collapse and compre of the posteriorly lying neural structures in the spin canal Paraparesis or paraplegia results Less ofte disease extending laterally into one or both psoas muscl compartments causes paraplegia or paraparesis by involving the outflowing nerves of the lumbar plexus Fe such cases, are considered here, and attention is draw to the features differentiating bilateral plexus lesions fro the more common cord or cauda equina compressions.

Study of the literature indicates that even unilater lumbar plexus lesions are uncommon in associat with psoas abscess

Case-reports

Case 1—A boiler fireman, aged 56, was admitted hospital on April 11, 1946, complaining of a dull ache in th left sacro iliac region for one year The pain was aggravat by bending forward and relieved by rest Latterly it h radiated down the posterolateral aspect of the left thigh calf to the lateral malleolus and had been accompanied stiffness in the lower back

Examination showed evidence of hypertension and arterio sclerosis The spine had a slight tilt to the right with marked restriction of mobility There was tenderness on pressure over the spines of the third, fourth, and fifth lumbar vertebræ, with reference of pain to the left buttock Motor power was deficient in the left glutei, hamstrings, posterior calf muscles and peronei On the right side there was weakness of the dorsi and plantar flexors of the ankle and of the peronei The left knee jerk was greatly depressed and the ankle jerk less so The right tendon jerks were normal There was sensory loss in either leg Straight-leg raising was limited on the left side to 60° with reference of pain to the left hip

Investigations—Lumbar puncture produced clear fluid under a pressure of 150 mm. There had be unsuccessful punctures elsewhere, and the yell thought to be explained by previous trauma Quec test was negative There was no increase in white and the total protein was 80 mg per 100 ml The W reaction was negative for both blood and cerebrospinal (c s f) Radiography showed partial collapse of the body the fourth lumbar vertebra with considerable narrowing of disc space between the third and fourth lumbar No paraspinal abscess shadow was seen Pronounced arthritic changes *suggested that the condition* was of standing The provisional diagnosis was "com of the fourth lumbar body with a lesion of the third fourth intervertebral disc causing bilateral compression"

Progress—Arrangements were made for spinal dec sion of the affected roots, biopsy, and subsequent fusion The patient was later admitted to hospital for purpose, but by then his symptoms had subsided to extent that he wished to return to work There was weakness of the leg muscles Spinal movements had Tendon reflexes were still depressed in the left leg The pressure was now 100 mm , with normal dynamics. fluid contained 18 white cells per c.mm. Protein was per 100 ml

Age, hypertension, and symptomatic improvement together decided in favour of conservative treatment returned home and resumed work Five months later been well in the interval, he was admitted to a medic with hæmatemesis and melæna, and complaining of frontal headache and cough Signs of meningitis afterwards Intracranial pressure increased progressively l the cells in his c.s.f He lapsed quickly into coma and ten days after admission.

cropsy showed in addition to the tuberculous meningitis n caused death a spinal lesion from which it took its n The fourth and fifth lumbar vertebræ were extensively d and replaced—mostly anteriorly—by soft caseous rial. From this lesion pus extended laterally into the tance of the psoas muscles on either side The lumbar es were not examined microscopically There was no dural extension of the disease The spinal cord and showed congestion of the pia mater but no surrounding late

ase 2 —A ploughman aged 28 a diabetic under treat t had a Brodie s abscess of the left femur drained on 17 1945 Four months later it had healed On Nov 20 he complained of low backache and pain radiating into sacrum. Next day it spread to both groins. The front e left thigh felt numb Two weeks later he was admitted to rgical ward with increased pain and a swinging tempera Large doses of penicillin did not control the infection. r days later he had difficulty in initiating micturition, and eloped severe abdominal distension He complained of kness of the thigh muscles and numbness of the front of h thighs.

xamination and Investigations—He preferred to lie on back with both hips flexed. Distension was too great to mit of successful abdominal palpation There was no spinal ormity and only slight tenderness on pressure or percussion r the mid lumbar spine In the lower limbs there was sting and bilateral flaccidity of the quadriceps muscles, h lesser wasting of the adductors of the thigh The anterior al group were still less weakened. Other muscle groups wed normal power. The knee-jerks were both absent and ankle-jerks preserved Plantar responses were flexor ere was bilateral depression to all modalities of stimuli r an area in the legs corresponding to the first second and rd lumbar dermatomes on the right and to the first second, rd and fourth lumbar dermatomes on the left Above d below this level sensation was normal Joint position se was unimpaired. Skiagrams of the lumbar and thoracic ines were normal The white-cell count was 20 000 per nm.—mostly polymorphs. Blood-culture was sterile tradural spinal abscess was diagnosed

Management and Progress—The extradural space was plored by excision of the ligamentum flavum bilaterally tween the eleventh thoracic and first lumbar levels. Condi ons there were found to be normal with fat of the usual nsistency and a normally pulsating dura. A fine rubber theter passed freely upwards and downwards for 5 cm. in e epidural space Exploration was also carried out between e third and fourth lumbar levels with negative results. umbar puncture at the close of the operation showed that ere was free conduction of fluid throughout the spinal eca. There was no increase of cells in the fluid and the otein content was 20 mg per 100 ml Attention was then cused on the affected nerves in their extraspinal course xploratory puncture revealed chocolate-coloured pus anterior o the lumbodorsal fascia in both loins. *Staphylococcus ureus* insensitive to penicillin was cultured Paralytic eus developed and the patient died two days later

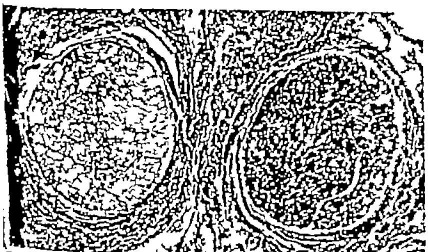

Fig 1—Section of the nerve trunks in case 2, showing inflammatory changes in the perineurium and patchy demyelination in one bundle (Anderson s stain, × 40)

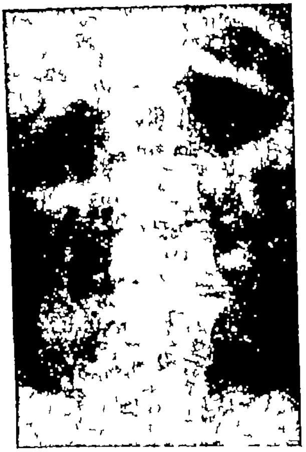

Fig. 2—Radiograph of the lumbar spine in case 3 showing the lesion in the bodies of the third and fourth lumbar vertebræ and calcification in a right-sided psoas abscess.

At necropsy in addition to the old abscess in the femur an area of eroded infected bone was found on the medial surface of the left ilium It formed a small part of the wall of massive abscess cavities in the sub stance of both psoas muscles the cavi ties communicated across the lower lumbar vertebræ and extended from the suprarenal glands to the pelvic brim The fifth lumbar body was destroyed anteriorly to a depth of 5 mm. and the fourth was affected to a lesser extent The abscesses contained pale chocolate-like fluid The sheaths of the lumbar nerves lying in the abscess cavities were swollen and congested. The autonomic nerves also lay in the abscess wall The spinal cord showed no abnormality Sections of the nerve trunks showed the epineurium to be involved in a subacute inflammatory process (fig 1) There was patchy demyelination and œdema around the fibres. The histological diagnosis was " pyogenic interstitial neuritis.

Case 3 —A housewife aged 26 suffered from bilateral pulmonary tuberculosis which was diagnosed in March 1946 In November, 1946 while under sanatorium treatment she began to complain of pain in the lower lumbar region radiating to the front of the right thigh.

Examination and Investigations—A psoas abscess was palpable in the right iliac fossa. There was spasm of the lumbar muscles and a lumbar kyphosis but no abnormal neurological signs in the lower limbs. Radiography showed erosion of the contiguous bony borders of the third and fourth lumbar bodies and narrowing of the intervertebral space (fig 2) The outline of the right psoas shadow was ragged the left was normal. Lumbar puncture produced clear c.s.f under normal pressure Queckenstedt s test was negative There were 2 cells per c.mm and 50 mg of protein per 100 ml This was taken to exclude intraspinal disease or at least to rule out the possibility of cord or cauda compression.

Treatment and Progress—The patient was immobilised and the abscess emptied by aspiration on three occasions. Amounts of pus up to 150 ml were withdrawn in which tubercle bacilli were seen. By June 1947 there was less spasm of the lumbar muscles and lumbar tenderness was not so severe, but considerable weakness of the right quadriceps muscles had developed and both knee-jerks were absent. There was no apparent motor weakness on the left side and no sensory loss in either leg An attempt to aspirate the abscess at this time was unproductive. A month later the patient complained of weakness of the left leg Examination then revealed loss of power in both quadriceps muscles, and some weakness in the hamstrings and the dorsiflexors of the ankles and toes. The weakness was greater on the right side There was sensory loss to all modes of stimulus over the third fourth, and fifth lumbar dermatomes on both legs The sacral segments were normal. Knee jerks were absent and ankle-jerks present The right psoas abscess was emptied again but an attempt to aspirate pus from the left psoas compartment failed Radiography showed little alteration in the vertebral disease but now there was evidence of disease in the left psoas muscle as well as in the right though no mass could be palpated on the left side

Further Progress—After aspiration of the right psoas abscess there was improvement in both legs. Power recovered in the right quadriceps first, and thereafter the right knee jerk returned A month later the left knee jerk had returned and no sensory abnormalities were demonstrable on either side More pus was aspirated from the right side on two occasions Further left sided aspirations yielded no pus, but a mass became palpable in the left flank Over the next six months progressively smaller amounts were removed from the right abscess and some calcification of its outline appeared in skiagrams Eventually there was no demonstrable neurological abnormality in the legs and this state of affairs has been maintained

Case 4 —A colliery washerman, aged 40, had suffered from tuberculous disease of the spine since childhood When first seen as an outpatient on Nov 5 1947, he complained of weakness of the ankles for one year and had adopted a high stepping gait to overcome this For two months he had experienced pain radiating down the posterolateral aspect of both buttocks thighs, and calves, and extending across the dorsum of the feet into the big toes Weakness spread to involve the knees and his gait became quite unsteady He was known to have had a right psoas abscess at the age of 8

On examination there was a gross kyphosis with its apex at the lower thoracic level No abdominal mass was palpable The left leg showed weakness of the external rotators of the hip and the hamstrings, with complete paralysis of the dorsiflexors and evertors of the ankle and weakness of the invertors On the right side there was a lesser weakness of the abductors and external rotators of the hip, of the hamstrings, and of all the muscles moving the ankle except the plantar flexors The knee jerks were depressed The ankle jerks were brisk and equal and the plantar responses flexor The abdominal reflexes were symmetrical but sluggish There was sensory depression to all types of stimuli in the fifth lumbar and first sacral dermatomes bilaterally The sensory loss was thus much less extensive than the motor

Investigations —Radiography showed lumbodorsal kyphosis with an angulation less than 90° The twelfth thoracic and first and second lumbar bodies were disintegrated and the upper half of the third lumbar body eroded—apparently recently The calcified lower end of a psoas abscess was seen on the right side

Progress —It was suggested that the referring surgeon should carry out a lumbar puncture to make sure that there was no spinal fluid obstruction and then empty the supposed psoas abscess by aspiration or operation Before this could be done the disease process extended Difficulty in micturition developed and with it anæsthesia in all sacral segments He was admitted to the neurosurgical unit with a complete paraplegia

Operation —Immediate decompression was carried out through an anterolateral approach Sequestrated disc and necrotic bone was removed from in front of the dura and an abscess evacuated from the right paraspinal region

Further Progress —After operation he required continuous bladder irrigation for fourteen days after which he passed urine normally Sensation in the sacral segments returned but depression persisted in the fifth lumbar and first sacral dermatomes bilaterally For some time there was spasticity in both legs but this disappeared in two months and the plantar responses became flexor again

Follow up examination nine months later revealed some weakness of the dorsiflexors and evertors of the right ankle and of the dorsiflexors of the toes There had been some return of power to the dorsiflexors of the left ankle but ankle evertors and the dorsiflexors of the toes remained paralysed The right knee jerk was weakly present the left absent Both ankle jerks were brisk and equal Plantar responses were flexor Bowel and bladder function was normal The weight was increasing and the erythrocyte sedimentation rate was normal All signs of cord compression had apparently disappeared and there was a return to the initial state showing bilateral involvement of the nerves of the lumbar plexus

This case is included with less confidence because the absence of C S F obstruction was not demonstrated initially Further involvement of the lower plexus roots is unusual and the lesion could possibly have been caused by epidural granulation tissue surrounding the lower [illegible]r roots intraspinally

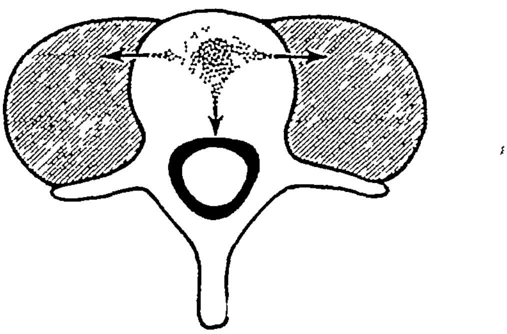

Fig 3—Diagram showing the relationship of a vertebral disease-focus to the spinal canal behind and to the psoas compartments on either side

Discussion

MECHANISM OF NEURAL INVOLVEMENT

Vertebral disease may spread in two directions to involve nerves—laterally into the substance of the psoas muscle or posteriorly to compress the spinal cord or cauda equina (fig 3) In assessing the probabilities reflected in bilateral neurological deficits in the lower limbs it must be remembered that a tuberculous focus in a body may spread into both adjacent psoas muscles without at the same time passing backwards This happened in the first three cases, but in the fourth bilateral spread occurred first and later was followed by posterior compression

DIFFERENTIAL DIAGNOSIS

Diagnosis should not be difficult on clinical grounds, provided the possibility of bilateral plexus lesions is remembered In cauda equina compression there will probably be bilateral symmetry and some involvement of the sacral roots Bladder dysfunction is almost invariable In plexus lesions neural involvement is usually asymmetrical and the sacral roots escape Bladder function is normal Case 2 complained of difficulty in starting micturition, but this was probably caused by involvement of the sympathetic nerves on the posterior pelvic wall Radiography *may show* the presence of psoas abscesses Lumbar puncture with Queckenstedt's test shows free C S F conduction if the lesion is extraspinal It should not be necessary to resort to myelography

Intrinsic spinal cord lesions should not be difficu to differentiate A glioma or angioma at the level of t second to fourth lumbar segments can cause lower mot neurone lesions like those of lumbar plexitis, and m even cause spinothalamic sensory defects with spari of the sacral dermatomes, but there will also be prese signs of pyramidal tract interruption causing increa of the ankle jerks and extensor plantar responses

Though all our cases had chronic infective lesio it is possible to imagine neoplastic conditions causi bilateral plexus involvement without intraspin extension

We have had under observation for four years a patient wi a myeloma of the tenth thoracic vertebra which had collapse She had a mixture of signs of spinal cord compression a lumbar plexus involvement When the spinal cord had be decompressed and the whole diseased area treated by radi therapy the sensory level of analgesia disappeared a bladder control was restored There remained lower mot neurone lesions causing flaccid paralysis below the knee which were almost certainly caused by infiltration or co pression of the lumbar plexus in its extraspinal course

NATURE OF THE PLEXUS LESION

In the only one of the four cases in which histologic material was available the nerve lesion was described a pyogenic interstitial neuritis. The epineurium was involved in a subacute inflammatory process and the fibre bundles showed œdema and patchy demyelination. This may be the common lesion.

Tallroth (1939) records a case of iliopsoas hæmorrhage in a hæmophiliac which was followed ten days later by signs of a femoral nerve lesion. He found no previous record of a similar case associated with hæmophilia. He points out that of the nerves in the psoas compartment the genito femoral obturator, and lateral cutaneous nerves are thinner and run more transversely and over shorter distances, than does the femoral which lies within the sheath all the way from its origin to the pelvic brim. The femoral nerve is therefore more vulnerable than the others. He suggests that the nerve lesion was caused by rapidly increasing pressure associated with an oozing hæmorrhage. In support of the pressure hypothesis he says that gravitational abscesses from tuberculous spondylitis do not cause femoral nerve lesions because the pressure rises slowly.

Michelson (1945) describes a case of trauma to the psoas muscle with hæmorrhage within the sheath and temporary impairment of sensation in the territory of the ilio inguinal nerve. Considering the cause of the nerve lesion he says

> Sudden increase of pressure within the psoas sheath due to hæmorrhage and/or infection may irritate the enveloped nerves sufficiently to produce symptoms of neuritis. Nerves are not involved with chronic slowly progressive lesions such as arthritis of the spine due to tuberculosis.

In Vuori's (1947) review of the condition of primary suppurative myositis in the psoas muscle there are no cases of neural involvement.

Schroeder (1938) describes five cases of primary psoitis none of which showed evidence of neuritis. This condition of primary psoas abscess usually staphylococcal in origin is the one in which neuritis would be expected whether the cause is increased pressure or inflammation.

Increased pressure within the psoas compartment bounded by an unyielding fibrous sheath appears to be a factor common to all the cases described. The four reported here make it clear that the increase of pressure does not require to be rapid as Tallroth (1939) and Michelson (1945) suggest. The histological finding of inflammatory changes in the lumbar plexus in case 2 does not necessarily mean that they had a causal significance in the production of neurological dysfunction. The absence of neurological signs in reported cases of acute suppuration in the psoas muscle indicates that toxic inflammatory changes in the nerve sheaths are unlikely by themselves to interfere with neural conduction.

We suggest that compression of the vasa nervorum of the lumbar plexus is the primary reason for the nerve changes. This should be relieved by closed or open drainage of the psoas compartment.

Summary

Bilateral neurological abnormalities in the distribution of the lumbar nerves may be caused by two paraspinal lesions as well as by one intraspinal lesion though the two will probably arise from one vertebral focus.

Four such cases are reported and the differential diagnosis and treatment discussed.

The cause of the plexus lesion is probably simple increase of pressure within the psoas compartment, and treatment should be directed towards lowering this pressure.

REFERENCES

Michelson E. (1945) *Arch. Surg Chicago* 50 77
Schroeder F (1938) *Acta chir scand.* 81 139
Tallroth, A (1939) *Ibid*, 82, 1
Vuori L. L. (1947) *Ibid* 95, 87

HEIGHT, WEIGHT, AND SKELETAL MATURITY IN THE FIRST FIVE YEARS OF LIFE

ROY M ACHESON
M A D.M Oxfd

F H KEMP
M B Birm F R.C P

JESSIE PARFIT
B.A M.D Lond

With the assistance of

EIRLYS JEFFERSON, M B Lond, M.R C.P
LAVINIA MYNORS, M B Lond
DAVID HEWITT, M.A

From the Social Medicine Unit Oxford University

SEVERAL communications from the Oxford Child Health Survey (see bibliography) have referred to the height, weight, and skeletal maturity status of the children but these measurements have not hitherto been reported in full. Compared with other ages there are very few height and weight tables for preschool children. It is also alleged that there is a secular change in the size of children of given age (Clements 1953). Measurements of skeletal maturity status are extremely rare, and the present assessments are not only the first to be based on British children, but also the largest series to be published anywhere.

The aims of the Oxford Child Health Survey were described by Ryle (1948) and full details of recruitment and conduct have since been published. The original group of Survey children were born (in Oxford) between 1944 and 1948 and some younger brothers and sisters have since been added to the series. All the children were examined at the age of 6 months and thereafter at six monthly intervals until they reached the age of 5. If, as a result of a mother altering the date of a clinical appointment any weight or height was recorded as long as a fortnight before or a fortnight after the correct date it has been excluded from the following tables. X ray findings were excluded if they were taken more than a month before or after the correct date. The vast majority of records were taken on the day the child reached the stated age.

Height (table I)

Height was measured with the child standing barefoot. A few babies could stand at the age of 12 months; but it was not until they were 18 months that as many as half the children were able to coöperate and not until 2 years that all the children could be measured.

TABLE I—STANDING HEIGHT (IN INCHES) OF OXFORD CHILD HEALTH SURVEY CHILDREN FROM 18 MONTHS TO 5 YEARS

Age (years)	Boys			Girls		
	No	Mean	S.D	No	Mean	S D
1½	134	31·86	1·30	120	31·09	1·20
2	251	33·05	1·39	202	33·19	1·27
2½	210	35·02	1·44	259	35·08	1·45
3	24[illegible]	37·28	1·60	263	36·71	1·46
3½	239	38·84	1·69	246	38·34	1·43
4	243	40·16	1·74	260	39·70	1·53
4½	224	41·62	1·79	238	41·01	1·60
5	234	42·75	1·00	238	42·38	1·72

Weight (table II)

When small the children were weighed naked and at later ages they wore only a single layer of underclothes.

Skeletal Maturity Status (tables III and IV)

Skeletal maturity was assessed in two ways. The first method was to compare the X ray films of the hands with the standard hand films for stated ages published in Todd's atlas (1937) This method, by giving "skeletal age" to the nearest six months (three months for the youngest children), yielded a rather coarse grouping from which it was not possible to calculate valid standard deviations However, the mean values shown in table III are probably satisfactory The second method of assessing maturity status, which is described in detail elsewhere (Acheson 1954b), dispenses with the concept of skeletal age and, in the form of "Oxford maturity units," provides skeletal maturation with its own yardstick This method yielded a relatively fine classification for the two hand films from which standard deviations, as well as means, could be calculated (table III) The same method was applied to both knees but in this case the frequency distributions were so irregular that they could only be characterised in terms of the mean and certain arbitrarily chosen percentile points (table IV)

DISCUSSION

In this country recent height and weight tables for the preschool child have been published by Gore and Palmer (1949) and by Low (1952) Neither of these sets of data are strictly comparable with ours Low's figures are based on a longitudinal study of 60 boys and 60 girls born in Aberdeen nearly thirty years ago These children were at all ages shorter and lighter than the Oxford children Gore and Palmer's study is also on a much smaller scale than the Oxford Survey, and is based on measurements taken in a single year, 1947 Every age-group consists of a separate sample of children, and within each one there are differences of weeks or months between the ages of the individual children These facts, preclude any exact comparison between their London children and the present series

TABLE II—WEIGHT (IN POUNDS) OF CHILDREN FROM BIRTH TO 5 YEARS

Age (years)	Boys			Girls		
	No	Mean	S D	No	Mean	S D
Birth	298	7 63	1 08	282	7 31	1 06
½	239	17 51	2 19	316	16 11	2 16
1	280	22 68	2 55	269	21 08	2 87
1½	299	25 44	2 93	285	23 90	2 99
2	290	27 76	3 23	289	26 14	3 40
2½	251	29 80	3 55	261	28 62	3 55
3	245	32 21	4 12	264	31 02	4 13
3½	211	34 60	4 67	246	33 21	4 28
4	213	36 75	4 90	250	35 60	5 04
4½	225	38 94	5 12	237	37 68	6 24
5	235	41 01	5 85	235	39 78	5 71

It will be noticed that the mean skeletal ages in table III are in every case less than the corresponding calendar ages That is to say, the Oxford children were behind the schedule of maturation drawn up by Todd for American children The mean skeletal age for g appears to overtake and pass that for boys, b it is thought that this results from an error the Todd standards for girls (Acheson and Hew 1954b)

TABLE III—SKELETAL MATURITY ASSESSED FROM X RAY FILMS OF HANDS AND WRISTS

Age (years)	No of children		Todd method mean skeletal age in months		Acheson method (in Oxford maturity units) for the two hands (left and right)			
					Boys		Girls	
	Boys	Girls	Boys	Girls	Mean	S D	Mean	S D
½	336	313	5 2	4 0	5 3	2 3	5 7	2 0
1	334	296	9 2	8 4	8 9	3 6	11 1	4 2
1½	315	306	14 6	13 [illegible]	13 8	4 7	18 4	4 9
2	313	305	20 8	18 2	18 9	4 7	23 4	4 6
2½	257	276	2[illegible] 1	24 8	23 3	5 3	27 6	4 8
3	268	270	33 1	32 7	27 1	5 7	31 5	6 1
3½	2[illegible]	252	37 4	35 3	30 6	5 4	35 7	6 7
4	265	261	42 2	45 0	33 5	6 4	40 0	7 4
4½	233	213	48 5	52 9	36 7	6 2	44 2	7 9
5	230	244	51·4	55 9	[illegible]0	6 9	48 1	7 9

TABLE IV—SKELETAL MATURITY ASSESSED FROM X RAY FILMS OF KNEES

(Measurements [in Oxford maturity units] for the two knees (left and right))

Age (years)	No of children		Boys		Girls	
	Boys	Girls	Mean	Spread	Mean	Spread
½	337	341	4 3	89 % at 4	4 5	82 % at 4
1	341	332	7 1	86 % at 6–8	7 5	77 % at 8
1½	313	303	8 2	82 % at 8	8 7	95 % at 8–1
2	304	300	9 4	86 % at 8–10	10 4	92 % at 8–1
2½	264	270	10 7	81 % at 10–12	12 3	89 % at 10–1
3	263	280	12 0	89 % at 10–14	14 3	81 % at 12–1
3½	263	251	13 2	83 % at 12–16	16 4	84 % at 14–2
4	260	250	14 6	84 % at 12–16	18 5	82 % at 16–2
4½	230	234	16 2	85 % at 14–18	20 2	73 % at 18–2
5	248	249	17 6	81 % at 16–20	21 5	88 % at 20–

Shuttleworth (1937) has emphasised that the ch value of longitudinal growth surveys is that th permit an accurate study of increments The Oxfo material is being examined from this point of vie and some of the findings have already been publishe At present a detailed study is being made of the effe of illness and adverse social circumstance on growth a skeletal development which, it is hoped, will throw furth light upon the process of maturation, and make possible to improve upon existing radiological metho of estimating maturity status

The Oxford Child Health Survey began in 1944 and r for ten years It was initiated by the late Prof John Ry and supervised at first by him and later by Dr Alice Stewa Dr Cicely Williams and Dr Celia Westropp bore the bru of the clinical and somatometric work, and Miss Elinor Robe and Miss Margaret Barnes shared the task of X raying t children From 1944 to 1950 the Survey was financed sole by the Nuffield Provincial Hospitals Trust, but from 19 onwards the Medical Research Council contributed generous towards its expenses

BIBLIOGRAPHY

Clements E M B (1953) *Brit med J* ii 897
Gore, A T, Palmer W T (1949) *Lancet*, i 385
Low, A (1952) Growth of Children University of Aberdeen
Shuttleworth F K. (1937) *Monog Soc. Child Dev* 2 no 5
Todd, T W (1937) Atlas of Skeletal Maturation St Louis

PREVIOUS PUBLICATIONS RELATING TO THE OXFORD CHILD HEAL SURVEY

Aims and Methods
Ryle, J A (1948) Changing Disciplines London
Stewart, A M., Russell, W T (1952) *Med Offr*, 88, 5

Breast feeding
Williams, E J (1947) *Publ Hlth* 60 201
Westropp C K (1953) *Brit med J* ii 138
Stewart, A M, Westropp, C K (1953) *Ibid* p 305

Social Data
Thwaites F J (1950) *Arch Dis Childh* 25, 193
— Sutherland, I (1952) *Ibid* 27, 60
Barber R, Blaschko M (1954) *Med Offr*, 91, 5

Clinical and Radiological Abnormalities
Cox N (1948) *Brit med J* i 148
Kemp I H (1950) *Brit J Radiol* 23 703
— Morley H M C Emrys Roberts E (1948) *Ibid* 21, 618

Physical Development Incorporating Radiological Data
Acheson R M. (1952) *Arch Dis Childh* 27 382
— (1954a) *Brit J Radiol* 27 298
— (1954b) *J Anat Lond* 88 498
— Jefferson E (1951) *Arch Dis Childh* 29 196
— Hewitt D (1954a) *Brit J prev soc Med* 8, 59
— — (1954b) *Hum Biol* 26, 343

Physical Development Other Growth Studies
Parfit J (1951) *Brit J soc Med* 5 1
Hewitt, D, Stewart A M (1952) *Hum Biol* 24, 309

CUTANEOUS VASODILATATION DURING FAINTING

E S SNELL
M.B Lond. M.R C P
SENIOR MEDICAL REGISTRAR

W I CRANSTON
M B Aberd , M.R C.P
ASSISTANT TO THE MEDICAL UNIT

J GERBRANDY*
M.D Amsterdam

From the Department of Medicine St Mary's Hospital Medical School London

It is now generally agreed that the fall in blood pressure during fainting results from peripheral vasodilatation rather than from any failure of cardiac function During venesection cardiac output decreases, but if a faint ensues output does not decrease further (Barcroft et al 1944) Lewis (1932) found that atropine abolished the bradycardia during fainting but had little effect on the hypotension or level of consciousness, and to emphasise the combined vagal and peripheral effects in these disturbances he used the term "vasovagal" attacks.

John Hunter (1793) observed that venous blood from the arm became bright scarlet during fainting McDowall (1938) ascribed pallor of the face to general cutaneous vasoconstriction and concluded that the explanation of Hunter's finding was vasodilatation in the muscles This hypothesis was seemingly confirmed by reports of vasodilatation in the forearm during posthæmorrhagic fainting (Barcroft et al 1944 Barcroft and Edholm 1945) and emotional fainting (Greenfield 1951) However measurements of skin blood flow during fainting have not agreed with each other (Weiss et al 1937, Barcroft and Edholm 1945, Rushmer 1944 Hertzmann 1954)

We have witnessed nine fainting attacks, which were mostly emotional in origin Measurements of heat elimination from the hand showed cutaneous vasodilatation invariably accompanied fainting

Methods

Heat elimination from the hand was followed by means of the calorimeter described by Greenfield and Scarborough (1949) The subjects were seated with the arm dependent Calorimeter temperatures ranged from 28 to 33°C but in any one experiment did not vary by more than 1°C Room temperatures were between 21 and 24°C and remained within ± 0 5°C during any one experiment During seven faints sublingual and rectal temperatures were measured by copper constantan thermocouples (Cranston et al. 1954), and blood pressure was recorded by the auscultatory indirect method in five faints.

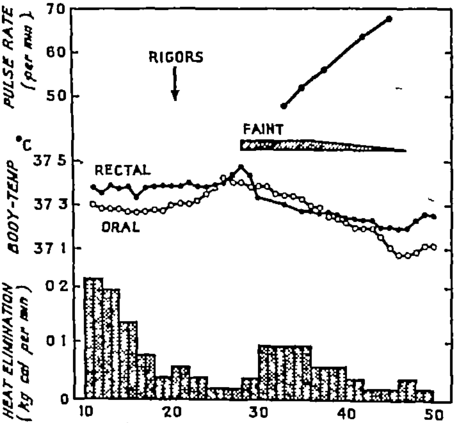

Fig 1—Pulse-rate, body-temperature, and heat elimination from hand in subject B.

In one healthy woman student (subject A) three faints were deliberately provoked by puncturing an arm vein with a sharp needle and withdrawing 5 ml. of blood she was seated on a high stool and the procedure was virtually painless The remaining six faints occurred in five men incidentally after the intravenous injection of bacterial pyrogens, which had been incubated in the subject's own blood (Gerbrandy et al. 1954a) (The pyrogens were injected therapeutically in three men with eczema and experimentally in two of ourselves) The volumes of blood injected were 10–50 ml. in four experiments and 200 ml. in two Four of the faints took place within ten minutes of the injection and at least forty five minutes before the onset of fever: the other two occurred twenty-eight and thirty five minutes after injection, during the onset of fever

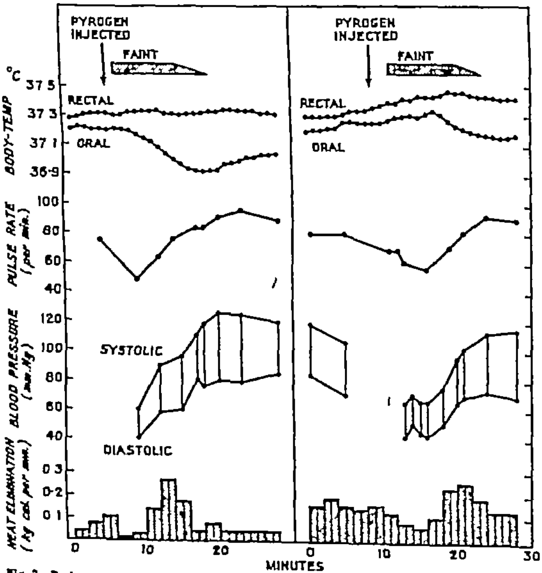

Fig. 2—Body-temperature, blood-pressure, pulse-rate and heat elimination in subject C.

Results

In none of the nine faints observed was there complete loss of consciousness. The first four faints observed were unexpected in all of them the pulse slowed and became irregular, but blood pressure was not recorded Heat elimination increased in all, including two subjects who were developing a fever with rigors and powerful vasoconstriction The observed changes in subject (B) are shown in fig 1, the abscissa of which represents the time after the injection of 50 million *Escherichia coli* in 16 ml of blood The ensuing fever was associated with a fall of heat elimination to very low levels rigors, and a small rise in mouth and rectal temperatures At this time he fainted the pulse rate was then 48 per min , and heat elimination increased to 0 09 calories per kg per min At the same time there was a fall in oral and rectal temperatures During recovery from the faint, heat elimination decreased and the pulse rate rose

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Subject C fainted on two separate occasions, after the injection of 50 million *Esch coli* in 30 ml of blood, and the results are shown in fig 2 Both faints took place at least forty five minutes before fever began During each attack there was a small transient decrease in heat elimination followed by a large rise , blood pressure, pulse-rate and oral temperature all decreased, while rectal temperature remained steady

The findings in the first experiment on subject A are shown in fig 3 First she witnessed a venesection on someone else about 50 ml of blood was run into a bottle and on to white towels This occasioned some emotional reaction but no fainting , the fall in heat elimination indicates cutaneous vasoconstriction, and there was a transient rise in systolic blood pressure 5 ml of blood was next withdrawn from a vein in the subject's own arm This provoked fainting, with weakness, clouding of consciousness, and pallor of the face, followed by sweating and hyperventilation The blood pressure fell by about 50 mm Hg and there was a small decrease in pulse rate and oral temperature Heat elimination rose from about 0 15 to 0 25 calories per kg per min

A further experiment on subject A is shown in fig 4 5 ml of blood was withdrawn from the subject, provoking a fairly severe and lengthy fainting reaction, with the same features as before Blood pressure fell to very low levels but there was only transient bradycardia Heat elimination rose to about three times its basal level, and stayed up until the blood pressure was increased by raising the legs The legs were again lowered, and this was followed by a milder faint with cutaneous vasodilatation during the period of hypotension

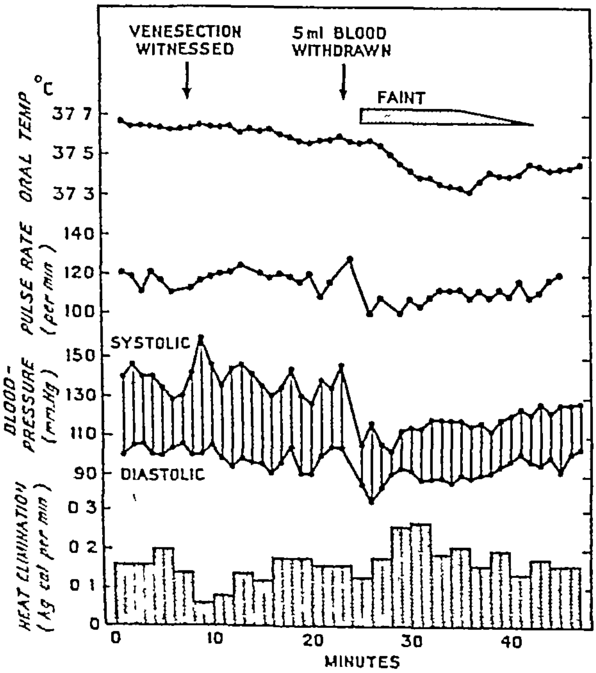

Fig 3—Oral temperature blood-pressure, pulse-rate and heat elimination in subject A.

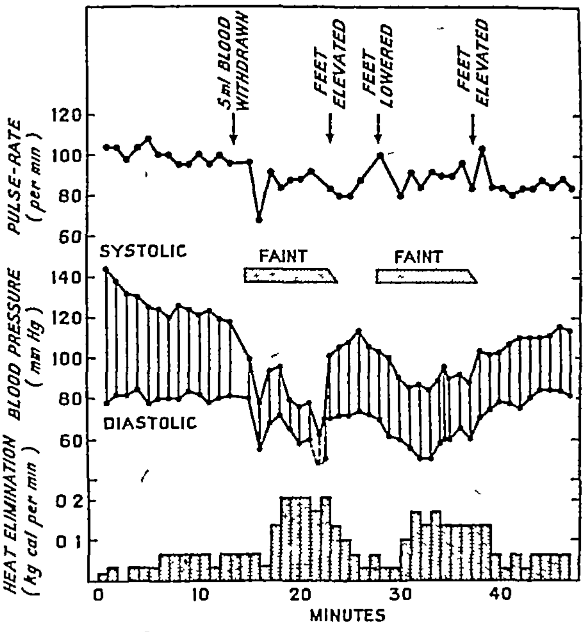

Fig 4—Observations on subject A

Discussion

The three faints observed in subject A were presumably almost entirely emotional in origin In the other subjects fainting occurred even if local anæsthesia had been given before the injection, so their responses cannot be entirely attributed to pain Fainting occurred in six out of forty six experiments in which pyrogen in blood was injected intravenously, and emotional factors are thought to have been mainly responsible for the attacks The general symptoms associated with the abrupt onset of fever may have played some part in precipitating the two faints twenty eight and thirty-five minutes after the injections

Normally there is loss of heat from the limb arteries to their *venæ comitantes* (Bazett et al 1948), and presumably also to other surrounding structures It is theoretically possible that the increase of heat elimination from the hand during fainting might be due to a rise in the temperature of the blood reaching the hand A slight rise in this temperature might result from vasodilatation in the forearm muscles, but this alone could not account for the observed increase in heat elimination It is much more likely that our findings indicate cutaneous vasodilatation in the hand during fainting This vasodilatation must be even grosser than the figures suggest, because it persisted in the presence of a lowered blood pressure Vasodilatation occurred even during periods of powerful cutaneous vasoconstriction, at the onset of fever It was not related to injection of pyrogen or blood, since similar increase in heat elimination was not observed in forty experiments of the same type in which fainting did not take place

There is a lag of at least one minute between the onset of vascular changes in the hand and any variations in recorded heat elimination, but otherwise calorimetry has fewer drawbacks than other methods as an index of skin blood flow during fainting The time relationships between changes in blood pressure and heat elimination (figs 1–4) suggest that skin vasodilatation contributes to the fall of blood pressure

Oral temperature invariably fell during fainting, but the extent of this fall does not necessarily reflect the effects of increased heat elimination on arterial blood temperature. We have previously observed during the onset of fever large falls in oral temperature with powerful cutaneous vasoconstriction (Cranston et al 1954); these changes were attributed to a reduction in the rate of blood flow through the mouth. The changes in oral temperature during fainting may be partly produced in the same way. Rectal temperature fell during one faint and was unchanged in the others, but it has been previously shown that rectal temperature responds poorly to changes in body heat (Gerbrandy et al 1954b). A decrease in cutaneous blood flow during fainting has been reported by Barcroft and Edholm (1945) and by Weiss et al (1937). Barcroft and Edholm induced fainting by reducing the circulating blood volume. Weiss et al used a combination of sodium nitrite and tilting. In both of these investigations blood flow was measured by a hand plethysmograph. During periods of hypotension the usual pressure in the collecting cuff may approach or exceed arterial pressure. Thus an artificially low blood flow may be recorded by this method. Barcroft and Edholm (1945) attempted to overcome this difficulty by decreasing the collecting pressure during the faint; the changes in blood flow which they depicted were inconstant, and were probably affected by the reduction of blood volume. In none of our experiments was reduction of blood volume induced by venesection or leg cuffs.

Rushmer (1944) followed the pulse volume in the finger during forty-five arterial punctures. Fifteen of his subjects fainted, though most of the punctures were painless and little blood was withdrawn. In all of these subjects pulse-volume increased during the faint. Hertzman (1954) recorded a similar observation in one case. This evidence is in favour of cutaneous vasodilatation during fainting.

The cutaneous vasodilatation during emotional fainting may affect forearm blood flow. Under resting conditions skin blood flow accounts for 0–67.5% of total forearm blood flow, and this proportion increases as skin flow increases (Cooper et al 1954). It therefore cannot be assumed that Greenfield's findings provide conclusive evidence for muscle vasodilatation during emotional fainting. Posthæmorrhagic fainting may be associated with different circulatory effects, and the increased forearm flow observed in this condition may be partly in the muscles.

Summary

Heat elimination from the hand has been measured during nine faints in six subjects. Six attacks followed intravenous injections of pyrogen in blood. Two occurred during the onset of fever, and the remainder were emotional in origin.

During all the faints cutaneous vasodilatation developed, judged by increased heat elimination from the hand.

Sublingual temperature fell during fainting, but with one exception rectal temperature remained constant.

Cutaneous vasodilatation contributes to the fall of blood pressure during emotional fainting.

We are indebted to Prof. G. W. Pickering and to Dr. G. Mitchell Heggs, physician in charge of the skin department, for permission to observe their patients who were undergoing fever therapy. We are also most grateful to subject A for her willing coöperation.

REFERENCES

Barcroft, H., Edholm, O. G. (1945) J. Physiol. 104, 161.
— — McMichael, J., Sharpey-Schafer, E. P. (1944) Lancet, i, 489.
Bazett, H. C., Love, L., Newton, M., Eisenberg, L., Day, R., Forster, R. (1948) J. appl. Physiol. 1, 3.
Cooper, K. E., Edholm, O. G., Mottram, R. F. (1954) J. Physiol. 123, 331.
Cranston, W. I., Gerbrandy, J., Snell, E. S. (1954) Ibid, 126, 34.
Gerbrandy, J., Cranston, W. I., Snell, E. S. (1954a) Clin. Sci. 13, 453.
— Snell, E. S., Cranston, W. I. (1954b) Ibid, p. 615.

References continued at foot of next column

PSORIASIS SPONDYLITICA

ERNEST FLETCHER
M.A., M.D. Camb., F.R.C.P.
PHYSICIAN IN CHARGE, DEPARTMENT OF RHEUMATOLOGY

F. CLIFFORD ROSE
M.B. Lond., M.R.C.P.
LATE MEDICAL REGISTRAR, DEPARTMENT OF RHEUMATOLOGY

THE ROYAL FREE HOSPITAL, LONDON

> *Essentia non sunt multiplicanda praeter necessitatem.*—
> William of Occam (d. c. 1349)

THAT psoriasis is particularly common in patients with rheumatoid arthritis has long been recognised, but a similar association between psoriasis and ankylosing spondylitis is not widely recorded. Cases of ankylosing spondylitis with psoriasis have—particularly in American accounts—been called "psoriasis arthropathica with sacro-iliac joint involvement." Coste and Forestier (1935) stated that it was rare to find ankylosing spondylitis complicated by psoriasis. Bouwens van der Boijens (1939) classified psoriasis arthropathica into eight types, one being the type associated with spondylitis; this he considered very rare. Epstein (1939) found 1 case of sacro-iliac joint involvement in 39 cases of psoriasis arthropathica. Of 150 cases of psoriasis arthropathica reported by Vilanova and Piñol (1951) 3 males had sacro-iliac joint involvement. They found that skin lesions were common over the trunk in spinal cases, and that these had a worse prognosis. Sherman (1952), reporting 15 cases of psoriasis arthropathica, noted 1 male who had had ankylosing spondylitis for forty years before the onset of psoriasis and peripheral joint involvement. Sterne and Schneider (1953), reporting 6 males with psoriasis arthropathica, mentioned 2 with sacro-iliac joint involvement; in both the peripheral joints were affected, but in only 1 did the skin lesion involve the trunk.

In 100 consecutive unselected cases of ankylosing spondylitis we found 4 with psoriasis. Since the incidence of psoriasis in the population is about 0.3% (Arnio and Clemmesen 1952) there would thus appear to be an association between ankylosing spondylitis and psoriasis comparable to that between *rheumatoid arthritis and* psoriasis. By analogy with psoriasis arthropathica this association may be called psoriasis spondylitica.

Case-reports

Case 1 was a woman, aged 39, who had developed psoriasis at the age of 11. When 25 years of age she complained of backache following the birth of her first child; this continued for fourteen years, becoming more severe with increasing limitation of spinal movement; latterly her right hip and shoulder had become painful. 3 brothers and 1 uncle had ankylosing spondylitis.

On examination her chest expansion was normal. There was a dorsal kyphosis, lumbar lordosis, and *limitation of* movement of the lumbar spine; she was unable to reach within 4 in. of her toes. There were plaques of psoriasis on both knees. The erythrocyte-sedimentation rate (E.S.R.) was 31 mm. in the first hour (Westergren). Radiography revealed squaring of the mid-dorsal vertebræ and irregularity and sclerosis of the sacro-iliac joints.

Case 2 was a man, aged 37, who worked as a post office clerk At 17 he had developed psoriasis 4 years later he complained of pain in both buttocks, localised to the ischial tuberosities and radiating down the backs of both thighs At the age of 23 he entered the Army and was placed in grade I, but a year later he again developed pains in the buttocks, these pains became severe and he was transferred to grade III A few months later he was referred to a psychiatrist and was discharged from the Army with "rheumatism and nerves" When he was 24 he began to have pain between the shoulder blades which was diagnosed as fibrositis and treated with infra red radiation and massage The pain in the buttocks and shoulder blades continued until the age of 29, when he developed pain and stiffness in the lower part of his spine, this was diagnosed as lumbago and treated with radiant heat The pain persisted until the age of 32, when ankylosing spondylitis was diagnosed He was treated with deep X rays with relief of symptoms His paternal grandfather, father, mother and a brother have psoriasis

On examination his chest expansion was 2 in, the spine was stiff, and he was not able to reach within 12 in. of his toes There was an upper dorsal kyphoscoliosis with obliteration of lumbar lordosis There were small patches of psoriasis on both elbows and knees The E.S.R. was 22 mm in the first hour (Westergren) Radiography revealed ankylosis of both sacro iliac joints and bambooing of the lower dorsal spine

Case 3 was a man aged 29, who at the age of 17 had developed psoriasis on the extensor surfaces of both forearms At 18 he entered the Army and was placed in grade I A year later he developed pain in his left hip, worse on sitting down, and at the age of 20 he was admitted to hospital with a diagnosis of tuberculosis of the left hip The following year the pain spread to his right hip and then to knees and elbows He was treated with gold injections but without improvement

At the age of 22 there was severe deterioration in his condition On examination at that time, the chest expansion was 1½ in, the skin was atrophic and there were plaques of psoriasis over the elbows and knees There was ulnar deviation of his hands, and his elbows were swollen, movements of the shoulders, hips and spine were severely limited The E.S.R. was 88 mm in the first hour (Westergren) Radiography of the pelvis showed obliteration of the sacro iliac joints The peripheral joints were treated with deep X rays but without improvement

At the age of 24 bilateral iritis developed and the patient became bedridden He was admitted to a chronic hospital where he now lies, aged 29, blind and completely helpless

Case 4 was a man aged 76, who had developed psoriasis at the age of 30 on both elbows and knees At the age of 64 he complained of stiffness of the neck and shoulders, low back pain and difficulty in walking He carried on work for four years until his hips became affected Radiographs at the age of 70 showed destruction of both sacro iliac joints and protrusio acetabuli of both hip joints He was treated with deep X rays with some improvement A maternal aunt had suffered from rheumatoid arthritis

On examination when he was aged 75 he appeared younger than his years There were patches of psoriasis on the left wrist and on the left buttock and natal cleft, and the movements of both wrists were limited The E.S.R. was 30 mm in the first hour (Westergren) At the age of 75 radiography of his hands showed destruction of the carpal joints, but the terminal interphalangeal joints were not affected

Discussion

Rheumatoid Arthritis and Psoriasis

The incidence of psoriasis in rheumatoid arthritis has been variously estimated at 2 6% (Dawson and Tyson 1938), 3 1% (Fletcher 1951), and 4% (Douthwaite 1935) Sherman (1952) stated that ulnar deviation is not seen in true psoriatic arthropathy and Epstein (1939) said that iritis is never found, but case 3, in which there was fulminating ankylosing spondylitis with peripheral joint involvement and psoriasis, showed both these complications

Rheumatoid Arthritis and Ankylosing Spondylitis

Because in some 25% of cases of ankylosing spondylitis the peripheral joints are involved, and the macroscopic and microscopic appearance of the joints is the same in rheumatoid arthritis as in ankylosing spondylitis, ankylosing spondylitis is sometimes thought to be nothing more than rheumatoid arthritis affecting the spine But for the following reasons the two conditions are considered, at least in Europe, to be distinct

(1) *Sex incidence* —Whereas rheumatoid arthritis is commoner in females (3 1), ankylosing spondylitis is commoner in males (6 1)

(2) *Age incidence* —Rheumatoid arthritis may appear at any age, whereas *ankylosing spondylitis most often starts in* the 15–40 age group

(3) *Course and prognosis* —Ankylosing spondylitis is more benign, most patients being able to continue at work Rheumatoid arthritis is characterised by more frequent remissions and relapses, 15% of patients becoming bedridden

(4) *Treatment* —Rheumatoid joints do not respond to deep X ray therapy, whereas the involved joints in ankylosing spondylitis do

(5) *Complications* —Necrobiotic nodules are hardly ever found in ankylosing spondylitis, but some 20% of patients with rheumatoid arthritis are so affected Moreover the incidence of iritis is greater in ankylosing spondylitis—15% in ankylosing spondylitis as against 5% in rheumatoid arthritis.

Ankylosing Spondylitis and Psoriasis

Arnso and Clemmesen (1952) found psoriasis in 2 of 20 cases of ankylosing spondylitis—an incidence of 10%, which is far higher than the incidence of 4% in our own series Psoriasis usually appears before rheumatoid arthritis in psoriasis arthropathica (Sterne and Schneider 1953), and in each of the 4 cases reported here the psoriasis developed before the onset of ankylosing spondylitis, the skin lesions were confined in all 4 cases to a few plaques over the knees and elbows Some cases of psoriasis arthropathica have a distinct clinical pattern with involvement of the terminal interphalageal joints, which is rarely seen in rheumatoid arthritis without psoriasis, but in the 4 cases of ankylosing spondylitis with psoriasis reported here the spondylitis was clinically indistinguishable from ankylosing spondylitis without psoriasis

Genetic influences play a part in the ætiology of both ankylosing spondylitis (Jacobs and Rose 1954) and psoriasis (Lerner 1940), as is shown by the family histories of cases 1 and 2 The former had 4 relatives (paternal uncle and 3 brothers) with ankylosing spondylitis, but none with psoriasis, and case 2 had 4 relatives (paternal grandfather, father, mother, and brother) with psoriasis, but none with ankylosing spondylitis

Ankylosing spondylitis often remains misdiagnosed for many years In view of this we suggest that if a pati with psoriasis complains of pain referable to the locomo system, the sacro iliac joints should be radiographed

Summary

4 cases of ankylosing spondylitis associated w psoriasis are reported

The relationship of ankylosing spondylitis, rheumat arthritis, and psoriasis to each other is discussed

REFERENCES

Arnso F, Clemmesen S (1952) *In* Rheumatic Diseases Lond p 64

Coste F, Forestier, J (1935) *Rev Rhum* 2 556

Dawson M H Tyson, T L (1938) *Trans Ass Amer Phy* *53 303*

Douthwaite A H (1935) The Treatment of Arthritis and Sciati London p 20

Epstein, E (1939) *Arch Derm Syph*, *N Y* 40 547

Fletcher E (1951) Medical Disorders of the Locomotor Syst Edinburgh p 397

Lerner, C (1940) *J invest Derm* 3, 347

Jacobs J H, Rose F C (1954) *Brit med J* ii, 1130

Sherman M S (1952) *J Bone Jt Surg* 34A, 831

Sterne E H Schneider B (1953) *Ann intern Med* 38, 512

von der Boijens B (1939) La Rhumatisme Psoriatique Paris

Vilanova X, Pinol J (1951) *Rheumatism*, 7, 107

LYMPHOCYTIC CHORIOMENINGITIS IN THE NEWBORN

PROBABLE TRANSPLACENTAL INFECTION

G. M. KOMROWER
T.D. M.B. Manc., M.R.C.I
LECTURER IN CHILD HEALTH

B. L. WILLIAMS
M.B. Manc
ASSISTANT LECTURER IN PATHOLOGY

P. B. STONES
M.B. Lond M.P.H. Harvard
LECTURER IN BACTERIOLOGY

UNIVERSITY OF MANCHESTER

Two foci of lymphocytic choriomeningitis (L.C.M.) infection in Manchester were described by Duncan et al (1951) and since then other cases have occurred in these two areas The case here reported in a newborn is the first recorded in infancy and evidence is presented that infection was acquired during the last stages of intra uterine life The mother was resident in one of the areas mentioned

Case history

A baby boy was born on June 4 1954 His mother had borne three other children who had been perfectly normal and thrived well. The mother was admitted to hospital on May 27 1954 eight days before delivery with four days history of malaise headache and vomiting On the day of admission she experienced some suprapubic pain and frequency of micturition there was no dysuria but very little urine was passed

On examination she had a cough and fever (temperature 103.8°F pulse rate 130) and there were generalised signs of bronchitis the blood pressure was 120/80 mm Hg and the fauces were mildly inflamed. Otherwise the examination was stated to be normal.

Investigations—Blood-cultures, radiography of the chest Widal and Paul Bunnell reactions, and repeated cultures of the urine had not elucidated the cause of the mother's condition by June 4. So the baby was immediately segregated at birth and not again brought into contact with the mother who continued to have a hectic swinging temperature and was transferred to another hospital, where on June 16 twelve days after the delivery the diagnosis of benign L.C.M. was suggested on the basis of a slight increase of cells and protein in the cerebrospinal fluid (C.S.F.) This was subsequently confirmed serologically the complement fixing antibody titre of her serum rising from less than 1/2 to 1/64

The infant weighed 6 lb 1 oz. at birth and appeared to be normal, passing urine and meconium on the first day He seemed to be well for the first six days because he fed satisfactorily and was active having a normal Moro and grasp reflex; but he lost 10 oz. in weight and by the eighth day 1½ oz. more. By this time his temperature had begun to rise and he was sucking indifferently and was a little dehydrated.

Investigations and Treatment—Aureomycin therapy (25 mg four hourly) was started A white-cell count of 31 900 per c.mm. (polymorphs 20% lymphocytes 52%) suggested an active infection, and streptomycin 125 mg daily was added to the therapy Tube feeding was started and subcutaneous saline solution was administered. The general condition remained stationary until June 15 when the infant's condition deteriorated and he had a convulsion Examination revealed some neck stiffness. Cisternal puncture produced clear xanthrochromic C.S.F. containing 4000 red cells and 54 white cells per c.mm. (36 polymorphs and 18 lymphocytes per c.mm.) and protein 150 mg per 100 ml. The possibility of virus meningitis or inclusion disease was considered at this stage

Course—There was rapid deterioration in the infant's condition and in six hours time the fontanelle was bulging and the baby showed severe opisthotonos. Cisternal and ventricular taps on this occasion revealed evenly bloodstained C.S.F. indicating subarachnoid hæmorrhage and the child died three hours later on June 16 1954 aged twelve days. A necropsy was done by one of us (B. L. W.) next day

Necropsy Findings—The body was that of a mature male infant weighing 4 lb 15 oz. and showing some wasting and dehydration Petechiæ were present on the lower abdominal wall groins and scrotum The *skull* was healthy with normal fontanelles. The *brain* weighed 300 g and appeared swollen There was extensive subarachnoid hæmorrhage over the left cerebral hemisphere and in the cisterna magna. On section the third and fourth ventricles and both lateral ventricles were moderately dilated and contained blood; the cut surface of the brain showed faint yellow discoloration Situated in the occipital lobe of the right cerebral hemisphere lateral to the posterior horn of the lateral ventricle was an area of intracerebral hæmorrhage 2 cm. in diameter and communicating with the lateral ventricle Macroscopic examination of the *thoracic* and *abdominal viscera* showed no abnormality

Microscopy—At the site of intracerebral hæmorrhage there was destruction of the brain tissue adjacent brain tissue showed œdema capillary congestion and sparse infiltration by macrophages. Overlying the left cerebral hemisphere and in the cisterna magna was hæmorrhage into the subarachnoid space Remote from the intracerebral and subarachnoid hæmorrhage the leptomeninges were congested and the subarachnoid space showed moderately severe lymphocytic infiltration There was also lymphocytic infiltration beneath the ependyma of the third and fourth and lateral ventricles Occasional blood vessels showed sparse perivascular lymphocytic cuffing Other tissues showed no significant abnormalities No obvious cause was found for the intracranial hæmorrhage which was thought to be due either to direct trauma (this seems unlikely in view of the situation) or more probably to change of intracranial pressure following the first cisternal puncture

Virological Investigations—A specimen of C.S.F. taken from the infant on June 15 1954 was inoculated intracerebrally into mice from a L.C.M. free stock and intraperitoneally into guineapigs. Eight days after inoculation the mice were sick with symptoms described by Traub (1936) as typical of L.C.M. A suspension of brain material from sick mice of this group was specifically neutralised by L.C.M. immune serum Complement fixing antigen prepared from the spleen of one of the two guineapigs killed on the sixth day after injection was also specific for L.C.M. The second guineapig bled from the heart fourteen days after inoculation showed L.C.M. complement fixing antibody in its serum. L.C.M. virus was also isolated from four pools of house mice caught in the mother's home

Discussion

Transplacental infection with L.C.M. virus has not hitherto been recorded although Traub (1939) and Haas (1941) have shown that it is the normal mechanism of infection in colonies of mice where the disease is enzootic.

In the present case since the infant was separated from the mother immediately after delivery no possibility of postnatal infection exists The possibility of paranatal infection must be borne in mind because it has often been stated that the urine in cases of human L.C.M. may contain the virus and thus the birth canal may have been contaminated Although it is well established that the virus is excreted in the urine of infected mice (Traub 1936) only one report has been published of the isolation of L.C.M. virus from the urine in man this is by Lépine and Sautter (1938) and appears to be of dubious validity

It therefore seems that transplacental infection was by far the most likely route in the present case particularly in view of the fact that the major phase of the mother's illness occurred at least a week before delivery In this connection it is of interest to mention that Swarts and Kercher (1954) have published a case of transplacental infection with poliomyelitis virus.

In further support of this view is the time of onset of the baby's illness. The incubation period of L.C.M. in man under natural conditions is extremely hard to establish because in most cases there is repeated exposure in the home environment van Rooyen and Rhodes (1948) give it as one to three weeks. In the two cases of laboratory infection reported by Milzer and Levinson (1942) and Lépine and Sautter (1938) the most likely times of infection were six and ten days respectively before the onset of disease though both cases were continuously exposed to the possibility of infection before these times In one of the cases of Smadel et al. (1942)

Case 2 was a man, aged 37, who worked as a post office clerk At 15 he had developed psoriasis 4 years later he complained of pain in both buttocks, localised to the ischial tuberosities and radiating down the backs of both thighs At the age of 23 he entered the Army and was placed in grade I, but a week later he again developed pains in the buttocks, these pains became severe and he was transferred to grade III A few months later he was referred to a psychiatrist and was discharged from the Army with "rheumatism and nerves" When he was 24 he began to have pain between the shoulder blades which was diagnosed as fibrositis and treated with infra red radiation and massage The pain in the buttocks and shoulder blades continued until the age of 29, when he developed pain and stiffness in the lower part of his spine, this was diagnosed as lumbago and treated with radiant heat The pain persisted until the age of 32, when ankylosing spondylitis was diagnosed He was treated with deep X rays with relief of symptoms His paternal grandfather, father, mother and a brother have psoriasis

On examination his chest expansion was 2 in, the spine was stiff, and he was not able to reach within 12 in of his toes There was an upper dorsal kyphoscoliosis with obliteration of lumbar lordosis There were small patches of psoriasis on both elbows and knees The E.S.R. was 22 mm in the first hour (Westergren) Radiography revealed ankylosis of both sacro iliac joints and bambooing of the lower dorsal spine

Case 3 was a man, aged 29, who at the age of 17 had developed psoriasis on the extensor surfaces of both forearms At 18 he entered the Army and was placed in grade I A year later he developed pain in his left hip, worse on sitting down, and at the age of 20 he was admitted to hospital with a diagnosis of tuberculosis of the left hip The following year the pain spread to his right hip, and then to knees and elbows He was treated with gold injections but without improvement

At the age of 22 there was severe deterioration in his condition On examination at that time, the chest expansion was $1^1/_2$ in, the skin was atrophic, and there were plaques of psoriasis over the elbows and knees There was ulnar deviation of his hands, and his elbows were swollen, movements of the shoulders hips, and spine were severely limited The E.S.R. was 88 mm in the first hour (Westergren) Radiography of the pelvis showed obliteration of the sacro iliac joints The peripheral joints were treated with deep X rays but without improvement

At the age of 24 bilateral iritis developed and the patient became bedridden He was admitted to a chronic hospital where he now lies, aged 29, blind and completely helpless

Case 4 was a man, aged 76, who had developed psoriasis at the age of 30 on both elbows and knees At the age of 64 he complained of stiffness of the neck and shoulders, low back pain, and difficulty in walking He carried on work for four years until his hips became affected Radiographs at the age of 70 showed destruction of both sacro iliac joints and protrusio acetabuli of both hip joints He was treated with deep X rays with some improvement A maternal aunt had suffered from rheumatoid arthritis

On examination when he was aged 75 he appeared younger than his years There were patches of psoriasis on the left wrist and on the left buttock and natal cleft, and the movements of both wrists were limited The E.S.R. was 30 mm in the first hour (Westergren) At the age of 75 radiography of his hands showed destruction of the carpal joints, but the terminal interphalangeal joints were not affected

Discussion

Rheumatoid Arthritis and Psoriasis

The incidence of psoriasis in rheumatoid arthritis has been variously estimated at 2 6% (Dawson and Tyson 1938), 3 1% (Fletcher 1951), and 4% (Douthwaite 1935) Sherman (1952) stated that ulnar deviation is not seen in true psoriatic arthropathy, and Epstein (1939) said that iritis is never found, but case 3, in which there was fulminating ankylosing spondylitis with peripheral joint involvement and psoriasis, showed both these complications

Rheumatoid Arthritis and Ankylosing Spondylitis

Because in some 25% of cases of ankylosing spondylitis the peripheral joints are involved, and the macroscopic and microscopic appearance of the joints is the same in rheumatoid arthritis as in ankylosing spondylitis, ankylosing spondylitis is sometimes thought to be nothing more than rheumatoid arthritis affecting the spine But for the following reasons the two conditions are considered, at least in Europe, to be distinct

(1) *Sex incidence*—Whereas rheumatoid arthritis is commoner in females (3 1), ankylosing spondylitis is commoner in males (6 1)

(2) *Age incidence*—Rheumatoid arthritis may appear at any age, whereas ankylosing spondylitis most often starts in the 15–40 age group

(3) *Course and prognosis*—Ankylosing spondylitis is more benign, most patients being able to continue at work Rheumatoid arthritis is characterised by more frequent remissions and relapses, 15% of patients becoming bedridden

(4) *Treatment*—Rheumatoid joints do not respond to deep X ray therapy, whereas the involved joints in ankylosing spondylitis do

(5) *Complications*—Necrobiotic nodules are hardly ever found in ankylosing spondylitis, but some 20% of patients with rheumatoid arthritis are so affected Moreover the incidence of iritis is greater in ankylosing spondylitis—15% in ankylosing spondylitis as against 5% in rheumatoid arthritis

Ankylosing Spondylitis and Psoriasis

Arnsø and Clemmesen (1952) found psoriasis in 2 of 20 cases of ankylosing spondylitis—an incidence of 10%, which is far higher than the incidence of 4% in our own series Psoriasis usually appears before rheumatoid arthritis in psoriasis arthropathica (Sterne and Schneider 1953), and in each of the 4 cases reported here the psoriasis developed before the onset of ankylosing spondylitis, the skin lesions were confined in all 4 cases to a few plaques over the knees and elbows Some cases of psoriasis arthropathica have a distinct clinical pattern with involvement of the terminal interphalageal joints, which is rarely seen in rheumatoid arthritis without psoriasis, but in the 4 cases of ankylosing spondylitis with psoriasis reported here the spondylitis was clinically indistinguishable from ankylosing spondylitis without psoriasis

Genetic influences play a part in the ætiology of both ankylosing spondylitis (Jacobs and Rose 1954) and psoriasis (Lerner 1940), as is shown by the family histories of cases 1 and 2 The former had 4 relatives (paternal uncle and 3 brothers) with ankylosing spondylitis, bu none with psoriasis, and case 2 had 4 relatives (patern grandfather, father, mother, and brother) with psoriasi but none with ankylosing spondylitis

Ankylosing spondylitis often remains misdiagnosed f many years In view of this we suggest that if a patie with psoriasis complains of pain referable to the locomot system, the sacro iliac joints should be radiographed

Summary

4 cases of ankylosing spondylitis associated wit psoriasis are reported

The relationship of ankylosing spondylitis, rheumato arthritis, and psoriasis to each other is discussed

REFERENCES

Arnsø, E, Clemmesen S (1952) *In* Rheumatic Diseases London p 64
Coste F, Forestier J (1935) *Rev Rhum* 2 550
Dawson M H Tyson, T L (1938) *Trans Ass Amer Phys* 53 303
Douthwaite, A H (1935) The Treatment of Arthritis and Sciatic London, p 20
Epstein, E (1939) *Arch Derm Syph N Y* 40 547
Fletcher, E (1951) Medical Disorders of the Locomotor System Edinburgh p 397
Lerner, C (1940) *J invest Derm* 3, 347
Jacobs, J H Rose F C (1954) *Brit med J* ii, 1139
Sherman M S (1952) *J Bone Jt Surg* 34A, 831
Sterne F H Schneider, B (1953) *Ann intern Med* 38, 512
van der Boijens B (1939) La Rhumatisme Psoriatique Paris
Vilanova X. Pinol, J (1951) *Rheumatism*, 7, 197

LYMPHOCYTIC CHORIOMENINGITIS IN THE NEWBORN

PROBABLE TRANSPLACENTAL INFECTION

G. M. Komrower
T.D., M.B. Manc., M.R.C.P.
LECTURER IN CHILD HEALTH

B. L. Williams
M.B. Manc.
ASSISTANT LECTURER IN PATHOLOGY

P. B. Stones
M.B. Lond., M.P.H. Harvard
LECTURER IN BACTERIOLOGY

UNIVERSITY OF MANCHESTER

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Summary

A case of lymphocytic choriomeningitis in a newborn infant is reported.

The probability of transplacental infection is discussed.

Our thanks are due to Dr C S D Don and Dr J W A Hunter for access to the mother's case notes, and to Dr M O Adams for doing complement-fixation tests on the mother's serum and for investigating the house mice.

REFERENCES

Duncan P R Thomas, A E Tobin J O H (1951) *Lancet*, i, 956
Haas V H (1941) *Publ Hlth Rep, Wash* 56 285
Lépine P Sautter V (1938) *Ann Inst Pasteur*, 61 519
Milzer A Levinson S O (1942) *J Amer med Ass* 120, 27
Smadel J E Green R H Paltauf R M, Gonzales, T A (1942) *Proc Soc exp Biol* N Y 49 683
Swarts C L Kercher E F (1954) *Pediatrics*, 14 235
Traub E (1936) *J exp Med* 63 533
— (1939) *Ibid* 69 801
van Rooyen C E Rhodes, A J (1948) Virus Diseases of Man 2nd ed New York

THE DIRECT FLOCCULATION OF INFLUENZA VIRUS

G BELYAVIN
M B Lond
SENIOR LECTURER IN BACTERIOLOGY, UNIVERSITY COLLEGE HOSPITAL MEDICAL SCHOOL, LONDON

By reason of its technical simplicity the direct agglutination reaction has been the serological technique of choice in both diagnostic and experimental bacteriology. In virology, however, its use has been restricted to the study of the plant viruses (Beale 1934, Bawden 1935), certain of the larger animal viruses, including the rickettsiæ (Otto and Dietrich 1917, Zinsser and Ruiz Castañeda 1932, Van Rooyen and Bearcroft 1943) and vaccinia (Ledingham 1931, Craigie and Tulloch 1931).

Agglutination of influenza virus was first reported over fifteen years ago (Magill and Francis 1938), but apart from additional observations by Henle and Chambers (1941) there has been no further development of this technique either as an adjunct to laboratory diagnosis or as a research tool. Such a possibility was suggested by the chance observation of typical flocculation in mixtures of highly purified virus and specific serum. I describe here the preliminary stages of an investigation designed to this end.

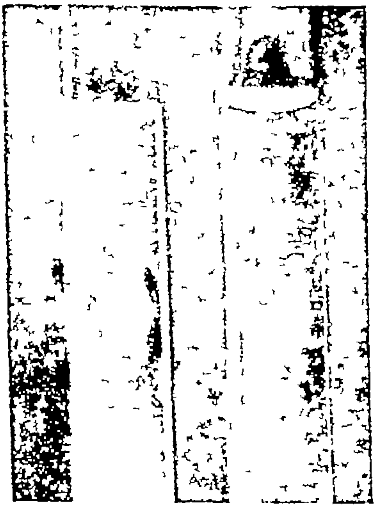

Fig 1—Fl... of eluate preparation of ... homologous antiserum ... 37°C.

Materials and Methods

Antigens

The following strains of influenza virus were used:

Type A PR8, received from the National Institute of Medical Research in 1947.

Type A "prime" FMI, obtained by the courtesy of Dr C H Andrewes from the World Influenza Centre.

MW, isolated in this laboratory in 1951 (Smith et al. 1951).

Ashby, isolated in this laboratory in 1953 and identified at the World Influenza Centre as a "Scandinavian" subtype (Isaacs and Andrewes 1951).

Type B Lee, received from the National Institute of Medical Research in 1947.

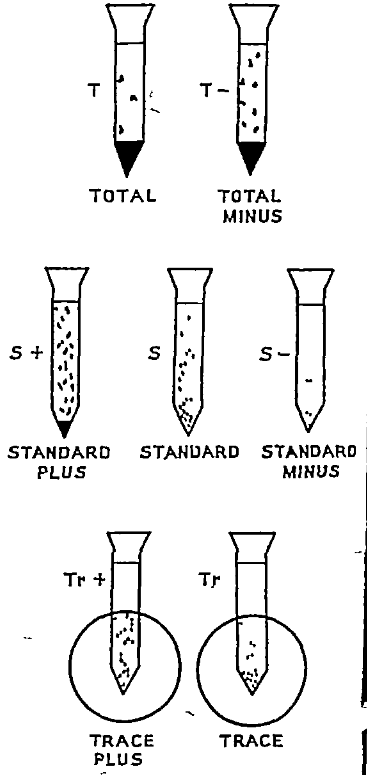

Fig 2—Defined degrees of flocculation of virus.

Viruses were grown by the allantoic inoculation of 11-day-old embryonated eggs with suitable doses of seed stocks kept at −70°C. They were used either as infected allantoic fluids or as partially purified and concentrated suspensions of virus in saline solution. Purification and concentration were achieved by either high-speed centrifugation or a single cycle of adsorption and elution from human red cells (Sheffield et al. 1954). Normal allantoic fluids clarified by centrifugation were also included as control antigens in certain experiments. When necessary, antigen preparations were stored at 2°C, and they retained their flocculability under these conditions for up to 6 or 8 months.

Sera

Rabbits were immunised by two intravenous injections of purified virus given at an interval of three weeks. The first injection was small, usually about 300 hæmagglutinating doses, and the second about ten times as great. Samples of serum were taken at convenient intervals after the first and second injections of antigen.

All the sera were inactivated at 56°C for 30 minutes and stored at −10°C without preservative.

Hæmagglutination

Virus antigens were conveniently standardised fo potency by hæmagglutination titration against fowl cel by the method of Belyavin et al. (1951). The titres serum which inhibited hæmagglutination by 4 agglutinating doses (A.D.) of virus were estimated by a simila technique.

Serum Absorptions

Virus, deposited from saline suspension by high spe centrifugation, was resuspended in appropriate aliquot of sera diluted 1/10 with physiological saline solutio and the mixtures were held at 4°C overnight. Next da the virus-serum mixtures were centrifuged at 22,000 for 1 hour to sediment the absorbing antigen. Th supernatant fluids constituted the absorbed antisera

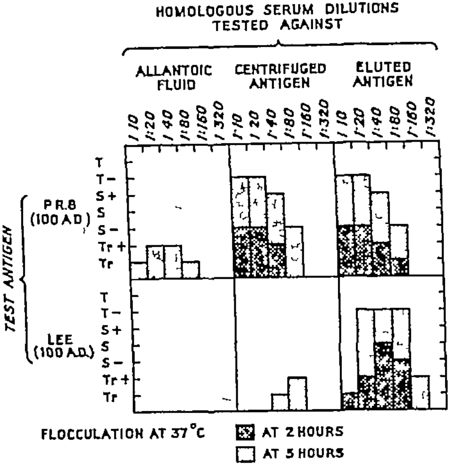

Fig 3—Relative speeds of flocculation of different preparations of influenza virus

Flocculation

Technique

Equal volumes (0 3 ml) of virus antigen and of serially diluted immune serum were mixed in Dreyer's tubes. The serum dilutions were pipetted first the virus antigen being added subsequently as in a bacterial agglutination test Orthodox controls containing only physiological saline solution and virus antigen were included in each test The rack was next placed in a water bath at 37°C the water level being adjusted to fall approximately between a third and a half of the way up the fluid column The tubes were inspected in a viewing box t short intervals

Development of Particulation

With suitable concentrations f antigen and serum there is a haracteristic sequence of events Within a few minutes after the tubes have been placed in the water bath at 37°C a faint opalescence develops which increases with time Eventually a fine granular precipitate forms; his is visible for a time only with a hand lens but develops subsequently into a well marked flocculation clearly visible to the naked eye It closely resembles a bacterial somatic agglutination (fig 1) the floccules sinking eventually to the bottom of the tube With a given antigen and antiserum a certain relative proportion of the two components gives the most rapidly particulating mixture and flocculation inhibition zones occur in the region of gross antibody or antigen excess Mixtures in the antibody excess zones usually show intense opalescence In these respects the reaction therefore behaves in the manner of a classical precipitin test Reduction of the amount of virus antigen added in a constant antigen titration leads to a smaller over all bulk of flocculum and the lowest concentration of antigen usable seems to be limited only by the detectability of the precipitate formed Antigen concentrations containing about 10–20 hæmagglutinating doses of virus per ml appear to be at the practical limit

Recording Degree of Particulation

In applying and studying this reaction it was found convenient to record the degree of flocculation observed in terms of a modified Dreyer's notation (Dreyer and Inman 1917) The defined degrees of flocculation are illustrated in fig 2

Effect of Virus Purification on Flocculation

Comparisons were made between the flocculability of infected allantoic fluid, high speed centrifugate, and eluted virus In each case an infected allantoic fluid was divided into three equal parts one part was clarified by centrifugation at 8000 g for 15 minutes one part was purified and concentrated fivefold by high speed centrifugation and the third part was treated by a single cycle of adsorption and elution also with fivefold concentration Samples of each preparation

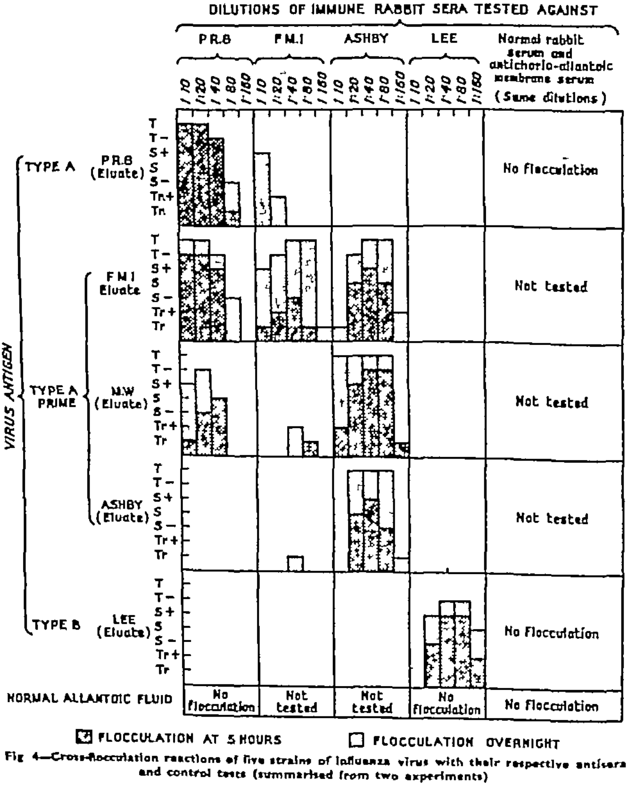

Fig 4—Cross-flocculation reactions of five strains of influenza virus with their respective antisera and control tests (summarised from two experiments)

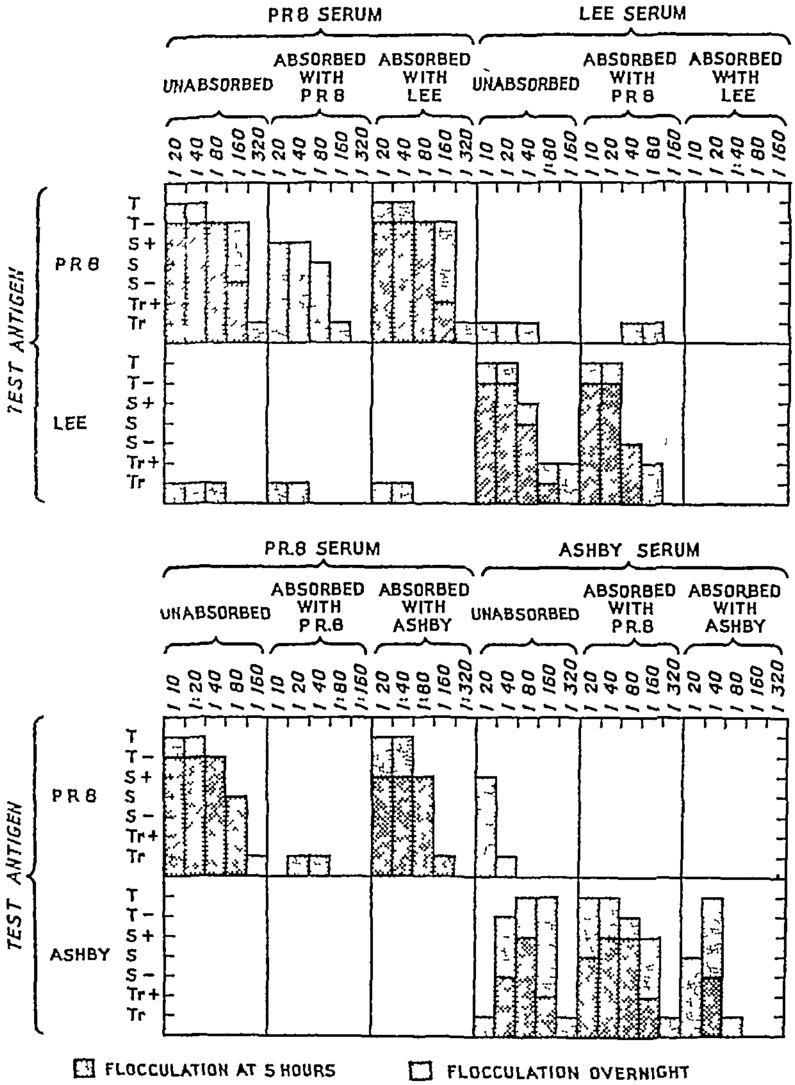

Fig 5—Results of two cross-absorption experiments using flocculation reaction to test absorbed sera.

adjusted by dilution to equivalent concentrations of virus in terms of hæmagglutinin, were compared for flocculability against serial bulk dilutions of homologous antiserum This was done using the PR8 and Lee strains, and an example of each (fig 3) shows the over all superiority of partially purified suspensions, which is notable in the case of some eluted preparations The poor flocculability of crude allantoic fluids relative to the purified virus suggests the presence of some material in the former which inhibits the reactions Probably such inhibitors present in crude preparations of virus explain the equivocal results of former workers

Experiments made with virus suspended in borate- and phosphate buffered saline solution showed that the rate and degree of flocculation were unaffected by differences of pH between 6 and 8

Specificity of Reaction

Reciprocal cross flocculation experiments were made with virus strains of distinguishable serological type and their homologous antisera In several of these experiments normal allantoic fluid, normal rabbit sera, and antisera prepared by immunisation of rabbits with saline extracts of normal chorio allantoic membrane were included as controls These latter were known to contain potent [illegible] fixing antibodies against membrane antig [illegible] ults of two such experiments (summarised in fig 4) show clearly the specificity of the reaction and the closenes with which it parallels the known serological pattern of the strains involved.

Serum Cross absorption Tests

The results of the cross-flocculation experiments were further confirmed by making reciprocal cross-absorption tests between viruses of distinguishable serological type and their respective antisera The absorbed sera were tested by full reciprocal cross flocculation reactions Two such experiments between a type A strain (PR8) and a type B strain (Lee) and between a type-A strain (PR8) and an A prime strain (Ashby) are illustrated in fig 5 These experiments fully confirmed the specificity of the direct cross flocculation experiments

Discussion

The experiments described show that the elementary particles of influenza virus are flocculated by specific antibodies Such a reaction has several practical applications A direct flocculation test of this nature, simple to perform and economical in apparatus and labour, will surely be of value in the routine serological typing of influenza virus Similarly, it may be applicable in the examination of post influenza convalescent sera and post vaccination sera, and a few preliminary experiments in this field encourage the view that this may be possible In a more academic field the technique provides another tool for the investigation of the nature and properties of the influenza viruses It may also be confidently anticipated that similar direct flocculation of many other animal viruses will be possible, provided that sufficiently purified and concentrated suspensions of virus can be prepared If they can, investigations of the effects of antigenic particle size on the dynamics of the specific precipitation reaction will be greatly facilitated For this reason, and in the hope of meeting urgent practical needs, the applicability of the present findings to the very small virus of poliomyelitis is now under investigation

Summary

The technique of a simple quantitative influenza vir flocculation test, using immune rabbit sera, is describe

The results of experiments which demonstrate i serological specificity and its inhibition by factors prese in normal allantoic fluid are presented, and the significance is discussed

I am indebted to Prof Wilson Smith for his critical advic The expenses of this work were defrayed by a department grant from the Medical Research Council

REFERENCES

Bawden F C (1935) *Brit J exp Path* 16 435
Beale H P (1934) *Contr Boyce Thompson Inst* 6 407
Belyavin G Westwood, J C N Please N W, Smith, W (1951 *J gen Microbiol* 5 546
Craigie J Tulloch W J (1931) *Spec Rep Ser med Res Cou Lond* no 156
Drever G Inman A C (1917) *Lancet* i 365
Henle W Chambers L A (1941) *Proc Soc exp Biol*, N Y 46, 713
Isaacs A Andrewes C H (1951) *Brit med J* ii, 921
Ledingham J C G (1931) *Lancet* ii 525

References continued at foot of next column

DEPOSITION OF IRON IN THE TESTES AFTER ADMINISTRATION OF AN IRON-DEXTRAN COMPLEX

J A. NISSIM
M.D Lond

SENIOR LECTURER IN PHARMACOLOGY IN THE UNIVERSITY OF LONDON AT GUY'S HOSPITAL MEDICAL SCHOOL, LONDON

PREVIOUS work with different iron preparations has shown that both the immediate and the later fate of iron in the body varies considerably depending not only on the size of the particle but also on the chemical nature of the non ionised compound (Nissim 1949 1953a) The study of iron uptake by the *testis in experimental siderosis* was stimulated by the earlier finding of a close correspondence in the distribution of saccharated iron oxide and of ascorbic acid in many organs (Nissim 1952a) It was found however that although iron appeared in a few histiocytes scattered among the interstitial tissue of the testis in a few days after the intravenous injection of saccharated iron oxide *most of the interstitial cells,* presumably endocrine remained entirely free from iron n later work moderate uptake of iron by the endocrine nterstitial cells was noted after repeated injections of he diffusible preparations ferric hydroxide ferrous ascorbate and ferric chloride caramelate (Nissim 1953b)

I report here the striking deposition of iron in the interstitial cells of the testis after the administration of the iron-dextran complex Imferon a deposition more massive than that in *any other organ in the body*

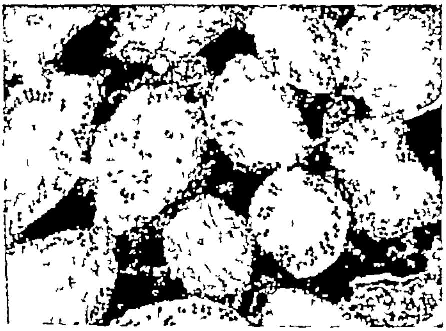

Fig 1—Testis of mouse showing massive deposition of iron in proliferated interstitial tissue with severe degeneration of seminiferous tubules and absence of spermatozoa after administration of 3 g of iron (as imferon) per kg of body-weight in six intravenous injections given twice weekly *Mouse was killed 11 weeks after last injection.* (Prussian-blue and carmalum. x 148.)

Methods

The iron-dextran complex was injected intravenously into white adult male mice in doses of 0 5 g of iron per kg of body weight weekly or twice weekly Some mice received similar doses subcutaneously Sections of the testes were studied at 3 4 and 24 hours, 4 days, and 2 weeks after single doses The total amount of iron given in repeated injections was 1, 2 and 3 g per kg of body weight and the mice were killed up to 10 weeks after the last injection

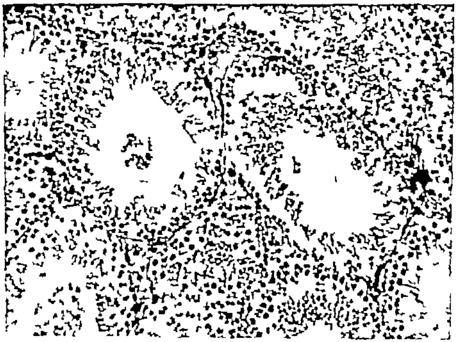

Fig 2—Testis of mouse showing heavy iron deposition in some interstitial cells and light staining of the rest of the interstitial tissue. *Note darkly staining fluid in one of the interstitial-tissue spaces.* Mouse received 0 5 g of iron (as imferon) per kg of body-weight in a single intravenous injection and was killed a fortnight later (Prussian-blue and carmalum. x 148.)

Results

All mice receiving repeated doses of imferon showed striking testicular atrophy, whose progress was followed easily by palpation The severity of atrophy depended on the total dose as well as the duration of siderosis The weight of testes showing maximal atrophy was 25–30 mg compared with 90–120 mg of the controls Sections revealed *increasing* degrees of iron *deposition* in the interstitial cells and correspondingly increasing damage to the seminiferous tubules with striking effect on spermatogenesis (fig 1) There was *in addition* an increase of interstitial tissue presumably as a result of replacement regeneration Tubule cells showed some iron staining in advanced interstitial siderosis.

Sections taken at intervals after single doses showed iron in the extravascular interstitial histiocytes as early as three hours after the injection when most of the iron was still in the circulation The prussian blue staining revealed in the interstitium spaces (figs 2–5) containing

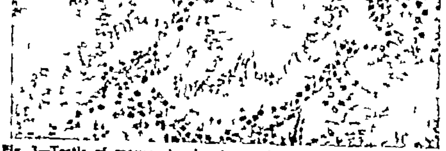

Fig 3—Testis of mouse showing heavy deposition of iron in some interstitial cells presumably mainly histiocytes, without staining *of the rest of the interstitial tissue* Note interstitial spaces containing fluid stained darkly with prussian-blue. Mouse received 0 5 g of iron (as imferon) per kg of body-weight in a single intravenous injection and was killed 4 days later (Prussian-blue and carmalum. x 148.)

DR. BELYAVIN : REFERENCES—*continued*

Magill, T P., Francis T jun. (1938) *Proc Soc exp Biol., N Y* 39 81
Otto R Dietrich, A (1917) *Dtsch med Wschr* 43, 577
Sheffield, F W Smith, W Belyavin, G (1954) *Brit J exp Path* 35 214
Smith, W Westwood J C. N , Belyavin, G (1951) *Lancet* ii 1189
Van Rooyen, C. E. Bearcroft, W G C. (1943) *Edinb med J* 50 257
Zinsser H., Ruiz Castañeda, M. (1932) *J exp Med* 56 455

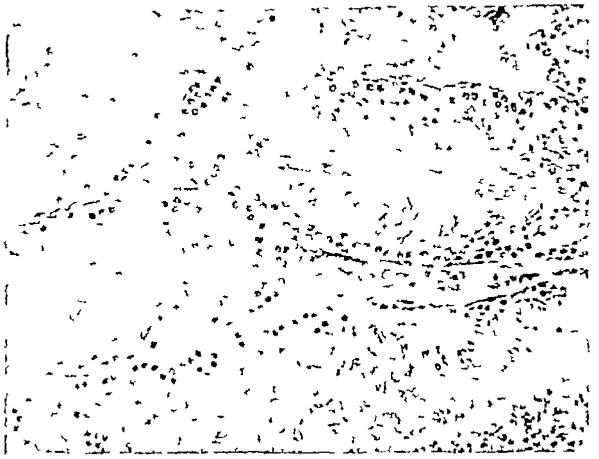

Fig 1—Testis of mouse showing uptake of iron by few histiocytes in the interstitial tissue, and blue-staining fluid in spaces In one space fluid surrounds a medium-sized vessel, which contains iron-staining plasma near the upper edge Mouse received 0 5 g of iron (as imferon) per kg of body weight in a single intravenous injection and was killed 4 hours later (Prussian blue and carmalum × 148)

fluid which bathes islets of interstitial tissue The staining in this fluid was initially as intense as that in the plasma, but, as the iron disappeared from the vessels, the fluid in the interstitial tissue spaces continued to show much iron staining With passage of time the endocrine interstitial cells exhibited increased iron staining and the number of cells with iron deposition comparable to that of histiocytes also increased These latter cells may be either proliferating histiocytes or the old endocrine interstitial cells that have become saturated with iron, but, since little histiocyte proliferation takes place in the testes after the administration of other iron preparations, the hypothesis of endocrine origin of these cells seems more likely

Discussion

Though these experiments do not suggest that a significant amount of iron may accumulate in the interstitial cells of the testes after therapeutic administration of imferon in man, the early appearance of the compound in the histiocytes and fluid spaces of the testes is possible In anæmia, however the iron is probably soon mobilised for the synthesis of hæmoglobin

Control experiments with saccharated iron oxide showed no iron in the interstitial histiocytes of the testes or in the fluid spaces until a few days after the injection, when some of the iron has been solubilised by the intravascular histiocytes which form the primary site of deposition Thus, the early appearance of imferon iron in the histiocytes and fluid spaces of the testes suggests a smaller particle size This was confirmed by the injection of the diffusible iron and ammonium citrate into mice Owing to greater toxicity the doses given were much smaller, but histiocyte uptake was shown as early as 1½ hours after the injection, and the fluid was visible in the interstitial spaces after an immediately lethal dose

The later stages in imferon siderosis lend themselves to ferent interpretations, but the continued presence staining fluid in the interstitial spaces suggests is continually transferred from the histiocytes ndocrine cells The progressive increase of the n in the interstitial tissue in turn suggests that also continually transported to the testes from arts of the body The iron compound apparently ers with the normal metabolism of the endocrine Whatever the mode of action the iron complex ges the seminiferous tubules and upsets spermato is The mode of action is a matter for further tigation

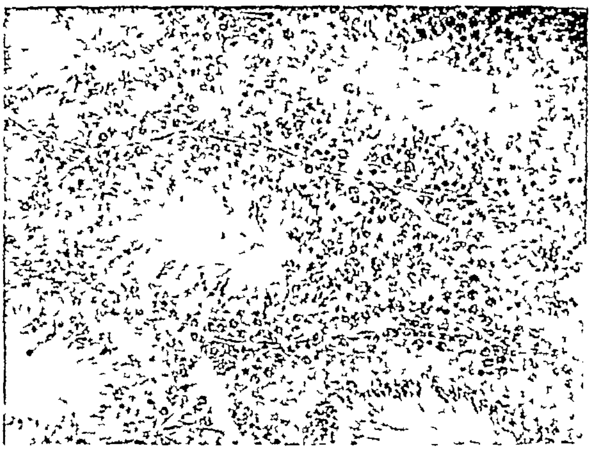

Fig 5—Testis of mouse showing absence of iron staining from a interstitial cells including histiocytes Compare normal seminiferou tubules and spermatogenesis with tubules in fig 1 Animal receive 0 5 g Fe /kg as saccharated iron oxide intravenously and was kille 4 hours later (Prussian-blue and carmalum × 148)

The deposition of iron in the testes after the adminitration of imferon reminds one of the deposition of iro in the testes and testicular atrophy in hæmochromatosis No deposition of iron has been noted, however, in th pituitary gland, the thyroid gland, or the islets o Langerhans after the administration of imferon, therefore the mechanism of the two conditions must differ

The ovaries of mice did not exhibit unusual affinit for imferon, the deposition of iron in them being simila to that described previously for saccharated iron oxid (Nissim 1952b)

Summary

Massive deposition of iron took place in the interstitia cells of the testes in experimental siderosis of mice wit imferon

This was associated with severe testicular atrophy an degeneration of the seminiferous tubules

I wish to thank Messrs Benger for the imferon used i these experiments

REFERENCES

Nissim J A (1949) M D Thesis University of London
— (1952a) *Brit J exp Path* 33, 419
— (1952b) *J Endocrin* 8 xxxix
— (1953a) *J Path Bact* 66 185
— (1953b) *Brit J Pharmacol* 8, 197 371

ACCIDENTAL INOCULATION WITH POLIOMYELITIS VIRUS

W F Twining McMath
M.D Belf, M R C P, D P.H
PHYSICIAN SUPERINTENDENT NEASDEN HOSPITAL, LONDON

The development of poliomyelitis in laboratory workers exposed to virus has rarely been recorded Sabin and Ward (1941) recorded the case of a laboratory associate, aged 35, who contracted paralytic poliomyelitis, probably in the course of her work on cynomolgus monkeys Two laboratory workers were reported by Beller (1953) to have been accidentally infected in the eyes and nose with Lansing virus while inoculating mice with a virulent mouse brain suspension, both developed symptoms after fourteen days

In the following case a technician was infected through accidental abrasion of a finger

A laboratory technician, aged 22, was admitted to Hospital on Nov 11, 1954 He had been employed in a research unit, and among his duties was the necropsy of animals dying after inoculation with poliomyelitis virus On Nov 1 he was removing the spinal cord from a monkey which had ecome paralysed and had died after repeated intramuscular oculation of a tissue-culture of propagated M.E.F 1 strain virus (type 2) The patient sustained a small abrasion of finger with a bone spicule from the vertebral column this ook three days to heal He was given gamma globulin 5 ml (1 5 g) intramuscularly on the same day and was uite well until Nov 9 when he complained of headache and umbar pain The following day he also had pain and enderness of abdominal muscles

On admission he had a temperature of 102 F slight neck tiffness, and a positive Kernig s sign. The neck stiffness leared up the next day, but the tenderness and spasm of bdominal and hamstring muscles continued for another week The erythrocyte-sedimentation rate was 1 mm in the first our (Westergren) White blood cells numbered 3800 per mm (70% polymorphs, 21% lymphocytes, 7% monocytes 2% eosinophils) Lumbar puncture was not carried out on dmission, but on Nov 25 the cerebrospinal fluid contained 250 lymphocytes per c.mm., 70 mg protein per 100 ml 720 mg chloride per 100 ml. and 70 mg sugar per 100 ml culture was sterile The complement fixation antibody investigations on serum taken on the third and twenty-eighth days of the illness did not by themselves lend convincing support to a diagnosis of recent systemic infection with poliomyelitis virus.

During the patient s illness there was indefinite weakness of the extensor muscles of the fingers of both hands His further progress was uneventful, and he was discharged for convalescence on Dec 12

Poliomyelitis was not epidemic in the district and it is reasonable to assume that the patient contracted poliomyelitis by infection through the accidental scratch The administration of gamma globulin on the same day as the injury did not prevent the illness from developing after eight days incubation though it may have lessened its severity

I wish to thank Dr W Wood for the history of the patient especially with reference to the administration of gamma globulin and Dr G L Le Bouvier, of the Virus Reference Laboratory Colindale for the serum complement fixation antibody investigations.

REFERENCES

Beller K (1953) *Zbl Bakt* 153 269
Sabin A B Ward, R. (1941) *Science* 94 113

Medical Societies

ROYAL SOCIETY OF MEDICINE

Osteoporosis

THE section of medicine met on March 22 with SIR HENRY COHEN the president in the chair to discuss Osteoporosis

Dr H A SISSONS defined osteoporosis as a condition of bone where the supporting tissue was reduced but remained highly mineralised and where sections did not reveal the broad osteoid seams which characterised osteomalacia Osteoporosis was a non-specific pathological response In examples of the local osteoporosis of disuse, where thin slabs of bone had been radiographed and then studied histologically the initial lesions were found to be localised areas of osteoclastic bone destruction in the chronic stage the changes were more diffuse and the porotic bone showed neither destruction nor formation of bone

In Cushing s syndrome an excess of adrenocortical hormone produced generalised osteoporosis The bony trabeculæ were thin and reduced in number excess osteoclasis was not apparent but osteoblastic bone formation was diminished Radiographs of slabs of the vertebral bodies showed that the trabeculæ at first lost their normal orderly arrangement and then broke under the force of compression so that the vertebral bodies collapsed

Dr Sissons regarded osteoporosis as an imbalance in the normal process of continuous bone destruction and formation in favour of destruction

Dr C E DENT discussed diagnosis He followed Albright s definition—a deficiency of the protein matrix of bone without abnormalities in the mineral elements The calcium phosphorus and phosphatase contents of the blood were normal He emphasised that the term was not to be used to cover any rarefaction of the bones which could result from osteomalacia (where the calcification of bone was at fault) from hyperparathyroidism (where there was an abnormal removal of calcium from the skeleton) or from neoplastic diseases of bone The diagnosis depended first on recognising that rarefaction of the skeleton had taken place The early changes were purely radiographic but collapse of vertebræ could be diagnosed by finding a reduction in the distance from the crown to the pubis which normally equalled that from the pubis to the heels and in the distance from the crown to the heels which normally equalled the span In osteoporosis some vertebræ were more rarefied and distorted than others in osteomalacia the vertebræ were more evenly affected The diagnosis of osteoporosis was by exclusion—a dustbin for those rarefactions of bone that could not otherwise be explained Some cases were indistinguishable from the late form of osteogenesis imperfecta

Dr Dent had not had much success with treatment in 4 cases of idiopathic osteoporosis which he had studied in detail but 1 had responded remarkably to repeated large infusions of plasma

Dr PAUL FOURMAN discussed endocrine aspects. The present-day definition of osteoporosis had been followed by several pupils of von Recklinghausen twenty five years ago Albright had sought to relate the condition to endocrine factors and had suggested that the failure of the bone matrix could be the result of a lack of anabolic hormones the N hormone of the adrenal cortex and the gonadal hormones it could, on the other hand, result from an excess of anti anabolic hormone, the 'S hormone of the adrenal cortex

Osteoporosis in old age was probably a manifestation of the normal atrophy of the tissues associated with ageing It could be perhaps related to a failure of adrenal N hormone production Senile osteoporosis was much commoner in women and when it appeared early it was called postmenopausal but Dr Fourman doubted whether it could be attributed to a lack of œstrogens, although œstrogens often relieved the pain The response to androgens was better still, but it was rare to find that the bones became denser

Dr Fourman demonstrated the osteoporosis of Cushing s syndrome and of acromegaly and mentioned the osteoporosis of diabetes Thyrotoxicosis did not produce osteoporosis as the speakers had defined it but it produced an excessive osteoclasis On the other hand cretins sometimes had osteoporosis and he had seen it in a patient with myxœdema He thought osteoporosis was a non-specific response to various different disturbances in the nutrition of the tissues

In the discussion Dr DONALD HUNTER emphasised that further advance depended on finding ways of measuring the changes. He appealed for the use of the band saw in the necropsy room Dr A W SPENCE agreed with Dr Hunter that in thyrotoxicosis there was excessive bone destruction He asked whether with methyl androstenediol one might achieve the same benefit as with androgens without the complication of masculinisation Dr B E C NORDIN suggested that the atrophy of the bones in osteoporosis might be in proportion to the atrophy of other protein tissues and that osteoporosis was but a symptom of disease affecting the whole body Insufficient attention had been paid to possible changes in the polysaccharides of bone matrix

Reviews of Books

Pædiatrics for the Practitioner

Vol I II, III and Index General editors WILFRID GAISFORD MD MSC, FRCP, professor of child health and pædiatrics University of Manchester, REGINALD LIGHTWOOD, MD, FRCP, DPH, director of pædiatric unit, St Mary s Hospital medical school London Butterworth 1955 Pp 1849 £13 10*s* the set

THIS ambitious work has now been completed by the publication of the third volume, the first having appeared in 1953 It epitomises the increasing emphasis on the promotion of good health in childhood, and is the first major pædiatric textbook to be written specially for general practitioners

It is comprehensive without being too detailed, and embraces such subjects as growth and development, the care of the newborn and normal child, social medicine, and psychology, as well as general medicine and surgery There are also chapters on disorders of the skin, eyes, ear, nose, and throat, and teeth The fifty two contributors, under the general editorship of Professor Gaisford and Dr Lightwood have concentrated on practical aspects, particularly the diagnosis and treatment of the common disorders of infancy and childhood, rare conditions are mentioned briefly to complete the picture Special attention is given to domiciliary treatment by the general practitioner, because the discovery of more potent drugs is increasing the proportion of illnesses which can be treated successfully at home This work is to be kept up to date by supplements which should enable the practitioner to keep abreast of changes

These volumes, well produced and liberally illustrated, should prove of great value to general practitioners in this important and satisfying field of medicine

Biochemical Determinants of Microbial Diseases

RENÉ J DUBOS, The Rockefeller Institute for Medical Research Cambridge, Mass Harvard University Press London Oxford University Press 1954 Pp 152 28*s*

THE substance of this book is a series of lectures given in 1953 on the occasion of the award of the Warren triennial prize of the Massachusetts General Hospital In *The Bacterial Cell* (1945) Dr Dubos examined some of the problems of infectious disease in relation to the form and habits of the parasites In this book his inquiry is directed to the part played by the host's internal economy in the prevention or encouragement of damage by the parasites Together the two works are a distinguished ornament to the "newer bacteriology" The keystone of the argument lies in the sentence " infection is in many cases the normal state, it is only disease which is abnormal" It is the end of the old anthropomorphic view that simplified all infectious processes to a war between an intact body and innumerable hostile invaders

Although much of the evidence is chemical the outlook is that of a biologist, and indeed some of the matter is drawn from fields outside the experience of most bacteriologists Dr Dubos modestly but sternly refuses to make dogmatic generalisations but throughout there flows a sparkling stream of suggestive hints and theses presented for disputation

It is a very proper book to put in the hands of him who imagines that all the fields for research are already under cultivation Others will regret their limitations of time and intellect but be grateful to the author for an exciting experience The writing is lucid if sometimes inelegant The make up is pleasant, but the price lamentably high

The Histopathology of the Respiratory Tract in Human Influenza

J F PH HERS, MD Leiden H E Stenfert Kroese 1955 Pp 77 17 50 Dutch florins

THIS is an excellent monograph It records a detailed examination of the epithelium of the respiratory tract in twelve cases of influenza, of which seven were complicated by infection with staphylococci and five with other bacteria The changes are compared with those found in four cases of fatal infection with *Hæmophilus influenzæ* and pneumococcus unassociated with influenza virus The coincident focal necrosis and regeneration is typical of, but not confined to, influenza, for the same appearances have been found in measles and varicella Examining smears of tracheal epithelium is valuable for rapid post-mortem diagnosis, and characteristic cytological changes can be recognised in the sputum during life The monochrome reproductions of the photomicrographs are good, and the method of placing them at the back of the book is unusual and effective

A Therapeutic Index

C M MILLER, MD Lond, MRCP, consultant physician, Sefton General Hospital, Liverpool, B K ELLENBOGEN, MD Lpool, MRCP, senior medical registrar, Royal Southern Hospital, Liverpool London Baillière, Tindall, & Cox 1955 Pp 148 12*s* 6*d*

IN this gallant attempt to compress modern therapeutic opinion into the space of a pocket-sized volume Dr Miller and Dr Ellenbogen have achieved comprehensiveness without undue sacrifice of detail no mean feat, for the territory is immense, the byways innumerable, and the main thoroughfares themselves sometimes hard to follow By describing only the more prominent landmarks (ancient monuments excepted) they have provided the young houseman or practitioner with a sensible and reliable Baedeker The book is likely to prove most valuable in emergencies, when there is no time to consult the larger textbooks, but it will also be read with profit in moments of leisure, for it contains some useful hints on practical procedures and therapeutic diets

Il Sistema Istiocitario

PIETRO FRANCESCHINI Florence Edizioni Scientifiche Salpietra 1954 Pp 883 L 12,000

THIS is a Florentine *cimento*, a " bold venture," by an anatomist and surgeon distinguished for his studies on the histiocytic tissue of synovial membrane, the reactivity of the peritoneum, and the histiocytic structure and function of the leptomeninges Dr Franceschini is a pupil of Chiarugi and Banti, and his book will interest specialists in many branches of physiology and pathology The book is a comprehensive account of the reticulo-endothelial system, and a valuable record of much fine, though little-known, Italian research

The first half deals with general topics, such as the relation of the reticulo-endothelial system to tissue permeability, blood coagulation, the destruction of erythrocytes, infectious diseases, antibodies, intermediary metabolism, occupational and systemic diseases, and antineoplastic resistance The second half is specialised, and includes chapters on the reticulo-endothelial system in the fœtus and placenta, skin, bone, synovial membrane, and peritoneum An appendix describes the part of the microscope in the history of biology Like many of his medical compatriots, Dr Franceschini has a historical sense, which he reveals with grace and modesty, with them he also shares a taste for controversy and a passionate concern for precise terminology, exemplified in a whole chapter on the definition of the reticulo endothelial system The chapter on Banti's disease will be of wide interest outside Italy It is a relief to find that we are not the only people who do not know what Banti's disease is, an Italian has concisely defined it as the tormented history of a genial pathogenetic conception

The book has 270 illustrations and ample subject and author indexes, it is well printed on good paper, and strongly bound

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Studies on Fertility —This sixth volume of the proceedings of the Society for the Study of Fertility, hitherto published in journal form, includes papers read at the conference held by the society in London last year The editor is Prof R G Harrison, DM (Oxford Blackwell Scientific Publications 1954 Pp 151 21*s*)

Fat Metabolism —The Johns Hopkins Press, Baltimore, has published a symposium on this subject, which was one of a series of conferences sponsored by the M & R Laboratories Columbus, Ohio The editor is Mr Victor A Najjar It is published in this country by the Oxford University Press (1955 Pp 185 36*s*)

THE LANCET

LONDON SATURDAY APRIL 2 1955

Nomenclature and Colon Disorders

STUDY of inflammatory conditions in the colon is bedevilled by the nomenclature, or the lack of it. Because of the naked-eye appearance of the large bowel of patients with chronic non-specific diarrhœa, WILKS and MOXON[1] introduced the term ulcerative colitis. The name having been given, the condition was assumed to be a disease *sui generis*. Consequently the question is not uncommonly asked: What is the cause of ulcerative colitis?; whereas the causes are probably many. There was BARGEN's bacillus; there is the school of allergy[2 3]; there is evidence that physical[4] and chemical[5 6] agents can precipitate the condition; and long ago SYDENHAM[7] stated: "Sometimes though very rarely it happens that a dysentery, not rightly cured originally, shall afflict a particular patient for many years"—an observation supported by STEWART,[8] FELSEN and WOLARSKY,[9] and HURST.[10] All these explanations may be right; certainly the histological evidence would support them all, for in the first instance ulcerative colitis appears to affect the mucosa, which like the skin may be subject to many forms of trauma and once severely damaged may remain unhealed.

Confusion has been increased by the response to the need for more titles. When CROHN[11] first described 14 cases of regional ileitis the name seemed to be no problem; but later it was realised that the colon could be involved, with or without a small-bowel lesion, and then the terms "regional enteritis" or "regional colitis" were brought into use. "Regional colitis" can also indicate ulcerative colitis proper; and BARGEN, who is convinced that ulcerative colitis starts in the rectum, has used this term for cases in which that organ is not involved. "Regional (segmental) colitis," he says, "may be defined as an inflammatory disease of unknown etiology involving initially one or more segments of the large intestine exclusive of rectum and recto-sigmoid, either as a continuous lesion or as multiple discontinuous lesions"[12]—a definition that includes both Crohn's disease and ulcerative colitis. Some may indeed regard with reserve the separation of Crohn's lesion from ulcerative colitis. Yet there are clear differences. To the naked eye they do not resemble each other; for, in contradistinction to the findings in ulcerative colitis, in Crohn's disease the bowel wall is thickened throughout all layers, the bowel tends to adhere to adjacent viscera and to become the site of fistulæ, and the limits of the lesion are well defined except for minute ulcers which are sometimes seen beyond the area of gross change.[13] The histological evidence of WARREN and SOMMERS[6] suggests that morphologically Crohn's disease is quite distinct from ulcerative colitis, while HADFIELD[14] maintains that in Crohn's disease mucosal ulceration is a secondary change not present at the outset. In ulcerative colitis the ileum may be involved as in Crohn's disease; but BROOKE[4 13] has shown that such involvement is incidental to the destruction of the ileocæcal valve by long-standing disease—a finding confirmed by INBERG.[15] Clinically, the complications of arthritis, iritis, and skin lesions are found only in ulcerative colitis. CROHN himself, reflecting on 562 personal cases, still feels justified in classifying the condition named after him as a pathological and clinical entity.[16]

COOKE and BROOKE[17] have now given a fuller account of a condition not unlike ulcerative colitis which they had already mentioned briefly.[18] Steatorrhœa is not a feature of ulcerative colitis even when the terminal ileum is invaded, unless there is associated pancreatitis. COOKE and BROOKE have seen 16 patients with frank steatorrhœa in whom there was radiographic and sigmoidoscopic evidence of colitis. In 2 cases diffuse ulceration of the small bowel was found at necropsy. There was little or no thickening of the wall of the small gut, and indeed there was no evidence of the lesion there until the intestine was opened for inspection. In this respect it differed from Crohn's disease. Ileitis secondary to ulcerative colitis is limited in extent and rarely involves more than a foot of intestine; but in their patients with steatorrhœa the small bowel was involved throughout. In the colon the right side seems to be attacked first; the inflammation then spreads distally. They therefore suggest that the colitis is secondary to the small-bowel disorder. The importance of this unusual condition lies in its close resemblance to ulcerative colitis—particularly that subgroup previously called right-sided colitis, which COOKE and BROOKE suggest, may be the same disease. The usual surgical treatment of ulcerative colitis proper may bring disaster in such cases; they argue that deaths from ileitis after ileostomy have included cases in which this condition was mistaken for ulcerative colitis and the small-bowel lesions passed unnoticed. Meanwhile yet another name has been added to the terminology; for what was at first called ileocolitis[18] COOKE and BROOKE now use the term non-specific enterocolitis. Ileitis secondary to ulcerative colitis could perhaps be suitably termed colo-ileitis, thus reserving ileocolitis or enterocolitis for conditions in which the small intestine is known to be affected primarily and the disease usually spreads distally.

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[1] Wilks, S., Moxon, W. *Lectures on Pathological Anatomy.* London, 1875.
[2] Andresen, A. F. R. *Rev. Gastroent.* 1951, 18, 779.
[3] Rowe, A. H., Rowe, A. *Ann. Allergy,* 1954, 12, 387.
[4] Brooke, B. N. Ulcerative Colitis and its Surgical Treatment. Edinburgh, 1954.
[5] Sloan, W. P., Bargen, J. A., Gage, R. P. *Gastroenterology,* 1950, 16, 25.
[6] Warren, S., Sommers, S. C. *J. Amer. med. Ass.* 1954, 154, 189.
[7] Sydenham, T. Medical Observations concerning History and Cure of Diseases. 1688.
[8] Stewart, G. T. *Brit. med. J.* 1950, i, 405.
[9] Felsen, J., Wolarsky, W. *J. Amer. med. Ass.* 1953, 153, 1069.
[10] Hurst, A. F., Knott, F. A. *Lancet,* 1931, ii, 1197.
[11] Crohn, B. B., Ginzburg, L., Oppenheimer, G. D. *J. Amer. med. Ass.* 1932, 99, 1323.
[12] Newman, H. W., Bargen, J. A., Judd, E. S. *Surg. Gynec. Obstet.* 1954, 99, 563.
[13] Brooke, B. N. *Lancet,* 1953, i, [illegible].
[14] Hadfield, G. *Ibid,* 1939, ii, 773.
[15] Inberg, K. R. *Act. chir. scand.* 1953, 106, 416.
[16] Crohn, B. B., Janowitz, H. D. *J. Amer. med. Ass.* 1954, 156, 1221.
[17] Cooke, W. T., Brooke, B. N. *Quart. J. Med.* 1955, 24, 1.
[18] Brooke, B. N., Cooke, W. T. *Lancet,* 1951, ii, [illegible].

Diuresis from Carbonic Anhydrase Inhibition

THE side effects of the early sulphanilamides included a metabolic hyperchloræmic acidosis[1] associated with alkaline urine[2] and increased urinary excretion of sodium and potassium[3 4] Later MANN and KEILIN[5] showed that sulphanilamide and its amino substituted derivatives inhibited specifically the enzyme carbonic anhydrase, which was demonstrated in the renal cortex[6] HOBER[7] linked these various observations by adding sulphonamides to fluid perfusing frog kidneys and showing that the normally acid urine was rendered alkaline by derivatives capable of inhibiting carbonic anhydrase PITTS and ALEXANDER[8] proved conclusively that acidification of urine depended on the active secretion of hydrogen ions into the tubular urine by cells of the renal tubules Sulphanilamide given to acidotic dogs both alkalinised the urine and increased excretion of bicarbonate bound base These studies, and their subsequent extension by PITTS[9 10] and BERLINER et al[11 12] have provided considerable insight into renal tubular mechanisms concerned with conservation of base It is now believed that one of the most important mechanisms by which Na^+ is reabsorbed from the glomerular filtrate is by exchange with H^+ and K^+ secreted into the lumen by tubule cells, whether the cation exchange of Na^+ is predominantly with H^+ or K^+ is apparently determined by the relative availability of these two ions within the tubular cells[13] Availability of renal-cell H^+ is determined by carbonic anhydrase through the following reaction sequence

$$H_2O + CO_2 \underset{\text{anhydrase}}{\overset{\text{carbonic}}{\rightleftharpoons}} H_2CO_3 \rightleftharpoons HCO_3^- + \underset{\substack{\downarrow \\ \text{secretory} \\ \text{exchange with } Na^+}}{\textcircled{H^+}}$$

Nothing is known of the biochemical mechanisms involved in the H^+/Na^+ cation exchange, but when available H^+ is reduced by carbonic-anhydrase inhibition or by reduction of CO_2 tension,[14] the over-all tubular reabsorption of Na^+ is reduced and sodium excretion increases Obviously, one way of promoting the renal excretion of sodium would be by deliberate inhibition of carbonic anhydrase

The possible therapeutic value of the diuretic action of sulphanilamide was recognised by SCHWARTZ,[15] who administered the drug to patients with congestive cardiac failure and recorded increased urinary output of sodium and potassium, together with significant loss of weight But, though the results were promising, the drug was too toxic in the large doses that were needed Since 1950 a relatively non-toxic heterocyclic sulphonamide, acet zoleamide (2 acetylamino-1,3,4-thiadiazole 5 s amide, compound '6063' or 'Diamox') has intensively investigated[16–26] Acetazoleamide is highly potent reversible inhibitor of carbon anhydrase which can be given by mouth[23] It absorbed rapidly and is stable in the body, it i excreted relatively slowly by the kidneys, and more than 70% of the administered dose is recovered in the urine within twenty-four hours[23] After a single dose of 250 mg the rate of excretion of sodium, potassium, bicarbonate, and water increases, the urine becomes alkaline, and excretion of ammoni and titratable acid is reduced[18 21 23 25] Which cation is principally excreted with bicarbonat depends partly on previous dietary intake, i potassium deficiency sodium-bicarbonate excretio is favoured,[13] and in sodium depletion potassium bicarbonate excretion[21] Toxic effects are uncommo and and slight[23] Drowsiness, or even quite dee sleep, has been experienced by some patients in mos large series studied[16 17 19 26], and apparently harmless paræsthesiæ, in the form of tingling or numbnes in hands and feet or about the mouth, are no uncommon[16 17 22 26] More serious cerebral symptoms such as toxic psychosis, are exceptional[23] Togethe with the other toxic symptoms, they suggest a direc action of the drug on the nervous system, they ar reminiscent of the occasional toxic psychosis an polyneuritis produced by the parent sulphanilamid The drowsiness and paræsthesiæ subside after withdrawal of the drug No peripheral motor symptom have been recorded Only one case of agranulocytosi has been recorded, the patient recovered[27]

It is thus evident that acetazoleamide has theoretic pharmacological qualifications as an oral diureti All workers agree that a single dose in healthy peop or œdematous patients will produce the diuret effects already described, the maximal rate and tot amount of bicarbonate excretion after a single dos show the usual logarithmic relation to dosage bot in man[21] and in the dog[23 25] But most worke also agree that the drug becomes ineffective o repeated administration, owing to the developme of hyperchloræmic acidosis[16 18 25 26] The diureti effect is determined by the amount of bicarbonat filtered by the renal glomeruli,[21 28] and either reduction in plasma-bicarbonate level or the reductio in glomerular filtration-rate that accompanies cardia failure will reduce the diuretic response Since th drug produces hyperchloræmic acidosis, it is self inhibitory, and, in balance experiments, continued administration produces no increase in sodium excretion after the first day, although a slight sustained negative potassium balance may result[18 21 25] At

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1 Southworth H *Proc Soc exp Biol N Y* 1937, 36 58
2 Marshall E K, Cutting W C Emerson K *J Amer med Ass* 1938 110 252
3 Strauss, M B, Southworth H *Bull Johns Hopk Hosp* 1938, 63 41
4 Beckman W W Rossmeisl E C Pettengill, R B Bauer W *J clin Invest* 1940 19, 635
5 Mann T Keilin D *Nature Lond* 1940 146 164
6 Davenport, H W, Wilhelmi A E *Proc Soc exp Biol, N Y* 1941 48 53
7 Hober R. *Ibid* 1942, 49 87
8 Pitts R. F, Alexander, R. S *Amer J Physiol* 1945 144, 239
9 Pitts, R F *Fed Proc* 1948, 7 418
10 Pitts R F *Amer J Med* 1950 9, 356
11 Berliner R W Kennedy T J Orloff J *Ibid* 1951, 11, 274
12 Berliner R W *Fed Proc* 1952 11 695
13 Evans B M Hughes Jones N C Milne M D Steiner, S *Clin Sci* 1954 13 305
14 Stanbury S W, Thompson A E *Ibid* 1952 11 357.
15 Schw [illegible] B *New Engl J Med* 1949, 240 173

16 Friedberg C K Taymor R Minor, J B, Halpern, M. *Ibid* 1953, 248 883
17 Belsky, H *Ibid* 1953 249, 140
18 Leaf A, Schwartz, W B, Relman W B *Ibid*, 1954 250 759
19 Relman A S, Leaf A, Schwartz W B *Ibid* p 800
20 Schwartz W B, Relman, A S, Leaf, A *Ann intern Med* 1955 42 79
21 Counihan, T B, Evans B M Milne M.D *Clin Sci* 1954, 13, 583
22 Ruskin, A *Arch intern Med* 1955, 95 24
23 Maren T H Mayer E, Wadsworth, B C *Bull Johns Hopk. Hosp* 1954, 95, 99
24 Maren T H, Ash V I, Bailey E M. *Ibid* p 244
25 Maren, T H, Wadsworth, B C Yale, E K, Alonso, L G *Ibid* p 277
26 Nadell J *J clin Invest* 1952, 32 622
27 Pearson J R Binder, C I, Neber J *J Amer med Ass* 1955 157 339
28 Schwartz W B, Relman, A S *J clin Invest* 1954, 33, 985

rst sight, therefore, the theoretical pharmacological ualifications are not borne out by clinical trial, ut, as often happens, clinical use introduces variables ot anticipated in the controlled experiment, and ublished clinical reports neither entirely support he pessimistic conclusions of the clinical investigator or agree with each other Consequently it is not yet ossible to assess the drug as a diuretic or to suggest uitable dosage Opinion on diuretic effectiveness aries from virtual nihilism [21] to considerable enthusiasm [16, 17, 22], and dosage has ranged from a single ablet of 250 mg, with at least a day between doses, o the continued administration of up to 6 g a day [22]

Amid this uncertainty a few points stand out learly With moderate continued dosage (up to 2 g a day in divided doses) no impressive diuretic response may be obtained in congestive cardiac failure due to hypertension or valvular disease [18, 21], but in "resistant" cases the drug may none the less alkalinise the urine and promote the excretion of large amounts of potassium [16, 21] This potential hazard should be borne in mind, and although potassium deficiency from this cause has not yet been recorded in man, it has been produced experimentally in the dog [23, 25] Patients previously resistant to mercurial diuretics may regain responsiveness when a relatively ineffective course of acetazoleamide has produced hyperchloræmic acidosis [19] Better therapeutic results seem to be obtained with moderate dosage in patients with congestive cardiac failure due to cor pulmonale [20, 24] a significant clinical diuretic response may ensue in about a half of such patients.[20] This better response is understandable if diuresis is determined by the load of bicarbonate filtered by the glomeruli The high plasma bicarbonate level in respiratory acidosis is determined by the high carbon-dioxide tension in the renal parenchyma [29] consequently it may be found that larger doses of acetazoleamide are needed to inhibit renal carbonic anhydrase in cor pulmonale The urine reaction and the rates of excretion of ammonia and titratable acid return to normal during continued acetazoleamide treatment [8, 21, 23, 25] and so although there is continued systemic acidosis there are no secondary effects on calcium and phosphorus metabolism such as occur with the hyperchloræmic acidosis of renal tubular acidosis.[23]

When acetazoleamide leads to a successful diuretic response in cor pulmonale [20] or in other types of congestive failure,[22] with weight loss and disappearance of œdema, it has obviously set off the renal excretion of chloride in addition to bicarbonate Nothing in the experimental investigations of the drug lead one to expect this effect, and there is need for careful documentation of the pattern of urinary excretion during the development of such responses Other aspects of chloride metabolism during acetazoleamide therapy warrant further investigation. The hyperchloræmic acidosis of continued drug administration develops without change in external chloride balance,[18, 21, 25] and it is usually ascribed to contraction of extracellular fluid volume after the renal loss of sodium bicarbonate yet the findings of LEAF et al.[18] suggest that a similar acidosis may ensue in patients showing diuresis only of potassium bicarbonate This explanation of the development of hyperchloræmia, and the identical explanation offered for the hyperchloræmia of renal tubular acidosis,[30] seem a little too facile It used to be thought that the hypochloræmia of potassium deficiency was the outcome of a negative chloride balance, we now know that this change may be associated with an actual chloride retention,[31] and during development of potassium deficiency chloride may be transferred into the inulin space from some other source of body chloride [32] Is it possible that shifts of body chloride take place during acetazoleamide therapy? Why should hyperchloræmia persist during therapy once the urine pH and excretion of ammonia and titratable acid have returned to normal? What renal change conditions this tolerance of a high plasma chloride level? These questions are far from purely academic, for we cannot hope to dispose of massive œdema unless we promote the excretion of chloride in addition to that of sodium.

Annotations

EFFECTS OF EXPOSURE TO NUCLEAR RADIATION

ON March 1 1954 a 'very large thermonuclear device' was exploded at Bikini an atoll in the western Pacific. The resultant cloud of radioactive material drifted down wind and eventually settled over a cigar shaped area some 220 miles long and up to 40 miles wide. Instruments had been placed at intervals over the predicted area of fall out enabling the American scientists to measure the intensity of the radiation at different points and to calculate the number of casualties there would have been had the area been populated They estimated that up to 140 miles down wind from the explosion the radioactivity would have sufficed to threaten the lives of all unprotected persons who failed to take any precautions whatsoever, 160 miles down wind, about half the number of unprotected persons might have survived, while 220 miles or more down wind even those exposed to the radioactivity for as long as forty-eight hours would have stood a good chance of survival [33] In actual warfare the number of casualties could be much reduced by taking immediate cover and also by prompt decontamination even such simple measures as thoroughly bathing the exposed parts changing the clothing and avoiding the ingestion of contaminated food may often save life Nevertheless, the predictions gave some idea of what a single large bomb might do—at least to an unprepared and uninformed population

As everyone now knows partial confirmation of the scientists' calculations was not long in coming On the day of the test a Japanese fishing vessel, the *Fukuryu Maru*, had been operating within 100 miles of the explosion The crew of 23 saw the flash, and observed a column of white cloud rising rapidly into the sky About three hours later a white powdery ash began to fall on the boat and it continued to fall for several hours After a few days, the fishermen noticed that those parts of their skin which had been touched by the ash had become dark red and swollen and on their return to port a fortnight later the entire crew was found to be suffering from radiation sickness They were admitted to hospital where their progress was studied by members of the clinical division of the Japanese Research Council of Radiation Sickness.

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29 Brazeau N Gilman A. *Amer J Physiol* 1953 175 33

30 Albright F, Burnett, C. H., Parson W Reifenstein, E. C Roos A. *Medicine* 1946 25 399

31 Black D A. K., Milne M D *Clin Sci.* 1952 11 397

32 Roberts, K E Randall, H T Philbin, P., Lipton R *Surgery* 1954 36 599

33 United States Atomic Energy Commission The Effects of High Yield Nuclear Explosions. Feb. 15 1955

The initial symptoms were the same as those which had been observed among casualties at Nagasaki and Hiroshima Some of the men began to have headache, vomiting, and diarrhœa within a few hours of their exposure to the ash, and in many of them depilation started before their return to port In the first month, exhaustion and anorexia were prominent symptoms, some developed fever of up to 102°F, and others showed a mild hæmorrhagic tendency Radiation dermatitis was present in almost every case Blood examinations in all cases revealed greater or lesser degrees of leucopenia, erythropenia, and thrombopenia, and an increase in the coagulation time, in 5 of the men the leucocyte count fell within the first month to 1000 per c mm In August one of the men developed jaundice, and he died on Sept 23 Extensive studies on the spermatozoa of the other 22 men showed in all cases a gradual reduction in the spermatozoa count, a diminution in the motility, and an increase in the proportion of deformed spermatozoa By last December (nine months after the Bikini test) the spermatozoa count had in every case fallen to zero

No aspect of nuclear radiation is at present causing more concern than the harm it may do to future generations Clearly, the effect of exposure to doses of any magnitude is to produce a serious disturbance of spermatogenesis, possibly leading to sterility which, though not permanent, may last more than two years (as in some of the Hiroshima and Nagasaki victims) But the real hazard is of course far more serious Radioactivity of all kinds has been found to cause an increase in the mutation rate in all animals and plants in which it has been tested, and, since most mutations of genes are harmful, the result of irradiation is that after several generations the incidence of abnormalities is raised Geneticists are still uncertain of the threshold level of irradiation below which the mutation rate is not increased, and conceivably this may be only a little higher than that produced naturally by existing radioactive material in the soil, water, and air What is known, however, is that as a result of the 60 odd nuclear detonations to date, the total radiation received by the world's population has measurably increased[33], and each future explosion will raise the total still further The exposure of each American citizen has been calculated as having increased by an amount equivalent to that received during one chest radiograph (0 1r)[33], in this country, it is said, the corresponding figure would be about a third of this[34] The point at issue, however, is not what radiation is being received by the chest but what radiation is being received by the gonads The doses in question are, of course, far lower than those which radiologists working with radioactive materials consider dangerous, but it has already been argued that, since vast numbers of the world's population are at risk, the possibility that the genes of some individuals have already been damaged cannot wholly be ruled out Opinion differs widely and Mr Iain Macleod, speaking for the Government, stated last week that the increase in radioactivity to date is most unlikely to have had any appreciable genetic effect But the fact that the *recent white paper on defence did not even refer to the* subject does not suggest any great eagerness on the part of the Government to supply discouraging information

Clearly the evidence is far from complete, as regards both the effect of radiation on the present generation, and the possible effects on generations in the future But, whether or not the test explosions have yet done any permanent harm to the human race, it seems likely that their continuance will eventually do so, for Prof Joseph Rotblat[35] calculates that explosion of hydrogen bombs at the modest rate of 2½ per annum would in thirty years double the natural level of radiation As for full-scale warfare with these weapons, he says that "it is no longer a question of two nations, or groups nations, devastating each other, but of all the futu generations of all nations who will for ever pay, thro disease, malformation, and mental disability for o folly"

ELECTROCARDIOGRAPHIC CHANGES IN INFARCTION

THE electrocardiographic diagnosis of infarction still depends on recognition of abnormal patterns in th twelve conventional leads Attempts by vector analy to integrate the deflections of body surface leads into single expression of the electrical forces of the heart ha proved informative, but this method is too complicat for clinical practice Grant and Murray[1] have propo a method by which the surface of the chest is divid into areas of positivity and negativity, and a simp correlation is established between the cardiac vector a the deflections of the electrocardiogram The deflectio of precordial leads can be compared with those produc at the surface of a cylinder by an electrical dipole at centre, and will be at zero when the axis of the lead perpendicular to the cardiac vector By plotting a num of zero points for different instants of QRS (0 01 se *0 02–0 04 sec) Grant and Murray constructed "a n* contour" on the chest of healthy people, with a positi area anteriorly and to the left and an extensive negati or "Q" area to the right and posteriorly

They found that the essential feature of infarction conventional electrocardiograms was the encroachment the Q area for the first 0 04 sec of QRS on to the left a anterior part of the chest From an admittedly sm number of cases they concluded that the mean 0 04 s vector was abnormal when it was directed 45° aw from and posterior to the mean QRS vector, or, anatomical terms, when it was directed away from t left ventricle instead of from the mitral/aortic orifi Comparing the electrocardiograms of 180 cases, Gra and Murray determined the "infarct vector" by su tracting the post infarction from the pre-infarction v tor, and found that it was directed away from t damaged part of the electrical field deforming the fi *0 04 sec of the QRS complex in almost every case* Th located the electrical defect in the heart by this meth and found fairly close agreement with the conventio anatomical localisation Divergencies with diaphragma and anterolateral lesions were probably due to the dire tion of the pre infarction vector Two types of alterati of the terminal 0 02 sec vector of QRS were found—o in a direction opposite to that of the initial vector, a the other in the same direction There was evidence su gesting that peri infarction block without QRS prolong tion was responsible for the former, and complete tra mural electrical defect for the latter The field defect all these cases of infarction was on either the anterior the diaphragmatic surfaces of the left ventricle and w distributed along the line of the interventricular septu

Grant and Murray insist that the electrocardiogra records electrical rather than anatomical localisation myocardial damage, and that the agreement wi empirical anatomical localisation is incidental The fa that even with multiple infarction there is only one area proves, they think, that each lead records the su of all the electrical forces at its particular point on t body's surface rather than the potentials of the unde lying myocardium Prinzmetal and his associates,[2] the other hand, strongly support Wilson's "window concept of the QS waves in infarction, in dogs wi infarction produced by coronary artery ligation, the recorded identical QS waves from epicardial, intramur and cavity leads over areas of completely functionle muscle But that this is not the only explanation of t QS complex was suggested by the rather unexpecte finding of similar cardiograms, differing chiefly in dep and steepness of the QS wave from infarcts where there was both clinical and histological evidence of some muscle activity Seeking another explanation Prinzmetal and his associates recorded direct electrocardiograms from parts of the ventricle which had been progressively damaged by burning or excision When only subepicardial muscle was damaged R waves were still recorded but when the outer third of the ventricular wall or the deeper areas were involved R waves were replaced by QS waves These observations suggested that the subendocardial muscle probably because of its rapid depolarisation contributes nothing to the R wave in an epicardial lead, and that QS leads can be produced by subepicardial as well as by transmural infarction Prinzmetal and also Grant and Murray confirm the practical diagnostic importance of QS waves and Q waves of 0 04 sec as signs of infarction but seem to contradict each other on the theoretical aspect The difference may be explained by the use of direct leads by Prinzmetal and of body surface leads by Grant and Murray This work helps to explain some of the limitations of cardiographic diagnosis

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[34] [illegible] 7 [illegible] March 23 19[illegible]

[35] B[illegible] *Atomic Scientists' Journal* March 1955 See *Guardian*, March 24

[1] Grant R P Murray R H *Amer J Med* 1954, 17, 587

[2] Prinzmetal M Kennamer R Maxwell M *Ibid* pp 610, 61

THE GREAT SCHISM

For some years microbiological circles have been stirred by a debate on the function of the bacterial flagellum, between Prof A Pijper on the one side and almost all the world on the other [1] This heretic believes that, far from being the organ of locomotion the flagellum is a trailing appendage of an automotive cell; and his evidence is formidable Oddly enough throughout the argument little attention has been paid to the detailed structure of flagella apart from some pictures from the electron microscope which are more elegant that informative Now Leifson and his colleagues [2] have shown that in stained preparations the flagella of proteus have in the main two distinct and well defined shapes. What they call normal' is an open spiral (or zigzag) of two to three waves curly' is a tighter spiral (or zigzag) of four to six waves The two may be found on different flagella of the same bacterium and there are two rarer types Which type is seen is influenced to some extent by the environment in which the bacterium has grown The wave lengths of each type of curve are remarkably constant for the same species of bacterium Almost simultaneously Pijper [3] has published a note on the same subject based as always on observation of the living bacillus illuminated on the dark field by sunlight He confirms his original statement that as a general rule the bacterium advances by a spiral movement of its body with the flagellum sticking straight out behind like an otter's rudder (In the photographs this always seems a bit fuzzy) Under circumstances which he has not yet defined this straight tail shortens and assumes a spiral shape which may have one of two wave lengths one twice as long as the other Initially the change is reversible but in the end the organ always finishes as a helix or splits into fine helicules These may whirl about for a short time and thereby give some erratic movement to the bacterium (quite distinct in Pijper's view from true motility) but their development is associated with stiffening of the body and final immobility

A cautious view suggests that these two reports describe the same phenomena modified by differences in method If the development of Pijper's helicules is always associated with death or at any rate immobility it is not surprising that they should be the structures seen in stained preparations He says that they may appear to move to any part of the cell wall which would explain the lophotrichous and peritrichous arrangements so loved by the systematists What he does not mention is whether these helicules retain the wave length of the helix from which they derive Leifson has carefully measured the wave lengths of his two forms of curve, but does not call attention to what is clear from his figures—that the wave-length of 'normal" curves is always about twice that of 'curly" In comparing results obtained by methods so different it would be unfair to ask for complete agreement, but it is a fair guess that Leifson's flagella are Pijper's helicules. Is the fuzziness of Pijper's rod like flagellum due to its being made up of a sheaf of flagellella ? And is this the beginning of the end of the great schism ?

THE EVIL SPIRITS

Many distinguished bacteriologists and immunologists have talked optimistically of the problem of infectious diseases as virtually solved and in his presidential address to the American Association of Immunologists,[1] Dr T P Magill has taken these people to task

Like Dubos, whose latest book is reviewed on p 704, he draws attention to our anthropomorphic attitude of mind He points out that the peaceful bacterium, trying to find food and shelter in man is termed an aggressor, whereas it is just as reasonable to call man the aggressor and that many of the manifestations of disease arise only when man tries to exorcise these supposedly evil spirits This viewpoint has virtues not the least of which is its recognition that the aim of preventive medicine should be less to eliminate an infection than to attempt to come to terms with it Attempts at elimination may have been less strikingly successful than the decline in mortality rates suggests It is galling to have to admit that the rates for tuberculosis, diphtheria measles and pneumonia began to fall long before modern preventive measures could have taken effect A factor that is often neglected in calculations on trends of an infectious disease is its natural history or ecology There are many examples of diseases which have ravaged populations until in the course of time they have lost their malignant character Such a change may be due to any of several causes Huge numbers of susceptible people may have died leaving a resistant core and in the microbial population it is the less virulent organisms whose survival is favoured since the organisms which kill their host have entered a blind alley The recent myxomatosis epizootics in Australia and in this country have shown such processes There are likewise examples of diseases regaining their former severity

Magill's lecture will have failed in its purpose if it encourages any ideas of nihilism public-health measures immunisation and antitoxin therapy are indispensable The lesson to be learnt is that infectious diseases are far from conquered and that present methods of controlling them are far from perfect In our pride at how much knowledge of bacteriology and immunology has been gained we must beware of becoming too complacent about the evil spirits

FOOD POISONING

The Public Health Laboratory Service has published another of its valuable annual reports on food poisoning in England and Wales This report on the year 1953 [2] contains an immense amount of data much of which is given in tables and it lacks the dramatic impact of the same facts described in narrative form In 1953 there were 5277 incidents—an increase of 1759 over the previous year These incidents consisted of outbreaks family outbreaks and sporadic cases The increase is reflected in all the causes listed—namely staphylococci Clostridium welchii undiscovered and particularly salmonella Better reporting must be taken into account, but by the most optimistic estimate there has been no decrease in food poisoning The authors of this believe that at least 4000 cases were not notif is a very high proportion

As in previous years meat dishes particular or made up meat dishes were the most impor but ham and boiled bacon were particularly important as vehicles of staphylococcal food-poisoning Milk caused 12 outbreaks, of which 7 were associated with fresh milk, 4 with dried milk, and 1 with canned milk 3 of the fresh-milk outbreaks were caused by *Salmonella typhimurium*, 1 of these was due to infection of pasteurised milk during bottling, and another to unpasteurised tuberculin tested milk 2 of the fresh milk outbreaks were due to *Staphylococcus aureus*, originating from infected cows Several outbreaks were associated with sweetmeats, and one of these, known to have affected two people, was associated with vanilla slices "*S enteritidis var danysz* was isolated from the patients and from mice in the bakery concerned The bakery had been baited with *S enteritidis var danysz* to clear it of vermin a month earlier"

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[1] See Lancet 1946, ii 871 Ibid 1948 ii 800; Ibid 1949 i 1013 Ibid 1952 i 88
[2] Leifson E, Carhart, S R, Fulton M, J Bact 1955 69 73
[3] Pijper A Nature Lond 1955 175 214

[1] Magill T P J Immunol 1955 74, 1
[2] Mon Bull Min Hlth Lab Serv 1955

The types of salmonella followed the same pattern as in previous years About 76% of cases were due to *S typhimurium* (aertrycke) with *S thompson*, *S enteritidis var jena* and *S bovis morbificans* next in order but accounting for only 7% of cases, the forty-six exogenous types accounted for 9% of cases *Cl welchii* food-poisoning was associated with meat dishes in every instance, except possibly 1 where the vehicle was not recorded

Fifty one deaths were recorded This report shows that food poisoning gives rise to a considerable amount of sickness with consequential loss of working time Much of this could be avoided by the education and co operation of the food handler We hope that the new Food Hygiene Advisory Council will accept as one of its first duties the education of the housewife, shopkeeper, restaurateur, and other food-handlers

CHIARI'S SYNDROME

THE clinical picture that results from occlusion of the hepatic veins is generally called after Chiari, who gave the first clear account of its pathogenesis[1], the disorder had first been reported by Lambron[2] some fifty years earlier From the number of published cases—115 by 1952—this syndrome might seem very rare, but this figure may be misleading, for Palmer[3] has reported 7 cases verified by necropsy and 4 presumptive cases all seen within a period of thirty-two months These cases were found at a large tumour clinic one of the commonest causes of the syndrome is encroachment by metastatic tumours on the hepatic veins, but since this is a late complication of malignant neoplastic disease it probably develops usually after the patient's discharge from hospital

The clinical features of the syndrome depend largely on the rate at which the hepatic veins are occluded In acute cases nausea, vomiting, and severe pain in the right hypochondrium due to rapid enlargement of the liver as a result of congestion may be quickly followed by death from hypotensive shock Less acute cases are characterised by severe and rapidly accumulating ascites and signs of portal hypertension with a developing collateral circulation Signs of hepatic failure are usually pronounced, and death results from hepatic coma Simultaneously developing œdema of the legs indicates involvement of the inferior vena cava in the occlusive process Chronic cases closely resemble hepatic cirrhosis, which may indeed develop as a result of the chronic liver injury due to the greatly impaired intrahepatic circulation Function tests invariably indicate severe parenchymal damage bromsulphalein excretion is much reduced, the serum albumin globulin ratio is reversed, and the flocculation test is almost invariably positive Patients rarely survive complete occlusion for more than a few months Ruptured œsophageal varices, portal or mesenteric thrombosis or intercurrent infection lead to death in the few who do n die of hepatic coma

Neoplastic involvement of the hepatic veins probab accounts for the majority of cases of Chiari's syndrom but occlusion of these veins or their ostia undoubte arises as a complication of many other conditio Palmer usefully classifies these under the follow headings congenital, mechanical, hæmatological, diffu and local liver disease, acquired vascular disease, an disease of neighbouring organs He lists some 42 c ditions as likely to be responsible for hepatic ven occlusion, of which 27 are known each to have accoun for one or more instances In patients severely ill w for example, leukæmia, cirrhosis, or local suppuratio chest or abdomen the syndrome may easily be overlook and even at necropsy the thrombosed hepatic veins easily missed if not specifically sought, and this r explain why published cases are so few

STRESS FACTOR IN THE DISC SYNDROME

WE may be on the threshold of important discove relating to the physiology and pathology of the in vertebral disc There is now evidence that the in vertebral disc is a hydraulic unit with a mechan generating an internal tension suited to the load impo on it The nucleus pulposus, exposed to isotonic saline, can generate considerable pressures (100–200 mm Hg) when resistance is offered to its swelling, and it is conceivable that an acute attack of lumbago might be due to disturbance of the mechanism controlling the access of fluid to the nucleus pulposus, with resulting tension—a possible parallel with the mechanism of acute glaucoma These speculations suggest possible explanations of the lumbago which follows exposure to cold and wet where there is no evidence of trauma

Scott[1] has described experimental evidence that swelling of the nucleus pulposus can be produced under the conditions of the "stress reaction" or "general adaptation syndrome"[2] The work reported by Scott was done on voles by D H Chitty, who exposed animals to strangers for about two hours a day for three or four days and then compared the size of the nucleus pulposus of each disc with that in control animals Statistical analysis showed that the difference between experimental and control animals was highly significant In support of the thesis that raised disc tension may be the basis of acute lumbago in man, Scott reproduces radiographs showing excessive hollowing of the opposing surfaces of vertebral bodies which enclose discs of rather more spherical shape than is commonly seen But many surgeons will regard this as a normal variation, commonly present without acute back pain, and in any case one would suppose it impossible for a vertebral body to adapt itself to a swollen disc in the three or four weeks during which the raised pressures of the acute tension episode are presumed to be present

We must here distinguish the difference in psychological states between patients with acute disc episodes and patients with chronic low-back pain Commonly, women who are depressed and unhappy subconsciously allow themselves to be disabled by pain of a degree which other women tolerate more or less easily Those who tolerate their discomfort do not tend to consult doctors, in other words, patients coming to hospital because of chronic backache are a self selected group On the other hand, in the case of really violent episodes of acute disc pain almost every patient seeks medical advice The experimental evidence of a "stress factor" relates essentially to acute disc episodes, but, though most surgeons would agree on the association of chronic backache with psychological disturbances, many will deny that this association is common in cases of acute disc lesions

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[1] Chiari H *Beitr Path Anat* 1899 26 1
[2] Cited by Budd G *In* Diseases of the Liver Philadelphia 1946
[3] Palmer E D *Ann intern Med* 1954, 41 266

[1] Scott J C *J Bone Jt Surg* 1955 37B 107
[2] Selye H The Physiology and Pathology of Exposure to Stre Montreal, 1950

Special Articles

MEDICAL ADVISORY MACHINERY OF REGIONAL HOSPITAL BOARDS

DOUGLAS HUBBLE
M.D Lond F.R.C.P

> I believe that a medical service cannot be effectively planned unless its organisation includes a comprehensive *and representative medical committee at regional hospital* board level This lack is one of the major defects of the present system. [1]

THESE words of the president of the Royal College of Physicians and the description of the effective machinery devised by the Liverpool Regional Hospital Board,[2] suggested that a survey of the methods used in other regions might be of interest

Of the 14 regional hospital boards in England and Wales 10 have a committee which whatever its title, corresponds in function to a medical advisory committee The constitution of these committees, their method of election and their method of reporting are set out in the accompanying table The organisation employed in the four other regions is as follows

Sheffield—The medical members of the board sit as the medical committee of the board Specialist advisory committees report to the board's medical committee Area consultant committees are consulted by and may advise the board

Birmingham.—A regional advisory committee composed of the chairmen of the group medical committees, sits to advise the senior administrative medical officer (S.A.M.O.) In addition there are advisory committees in each specialty

East Anglia—In each specialty there is an advisory committee to the S.A.M.O

North East Metropolitan.—22 advisory committees in the various specialties report through the S.A.M.O to the board Matters of general policy are referred where necessary to the advisory committee in general medicine

Thus the constitution of the medical advisory committees varies greatly, but most of the S.A.M.O.s express themselves as satisfied with their own organisation Although there are considerable geographical differences between the regions the methods of taking medical advice do not always seem to be the result of adaptation to environment There has however been at least one instance of evolutionary change in the South East Metropolitan region the medical advisory committee originally consisted only of the medical members of the board but it was later enlarged to make it more representative

In some regions the medical advisory machinery does not approximate to the ideal stated by Sir Russell Brain, and it does not always represent the clinical strength of the regional hospitals or of the medical schools. Even where a medical advisory committee is in being, it may not always be effective Sometimes its membership is too large and sometimes so small that it is unrepresenta

REGIONAL HOSPITAL BOARDS WITH MEDICAL ADVISORY COUNCILS

R.H.B.	No. of members	Including medical members R.H.B.	Description of other members	Method of appointment	Method of reporting	Frequency of meetings	Specialist advisory committees
Newcastle	15	Yes	Gen. practitioners (2) M.O.H. (1) Consultants (4)	Appointment after appropriate consultations	Planning committee R.H.B.	Fortnightly	Yes, panels of specialist advisers
Liverpool	23	Yes	University (3) Boards of governors (3) M.O.H. (1) Regional consultants (6) Coöpted (1) G.P (1)	Nomination by appropriate bodies	Planning committee R.H.B	Monthly	Yes
Leeds	11	Yes	Coöpted members (4)	Coöption	General purposes committee R.H.B.	Monthly	Yes, panels of specialist advisers
Manchester	20	Yes	Gen. practitioners (2) Regional consultants (6) Regional advisers and coöpted members (8)	Appointment after appropriate consultations	R.H.B.	Two-monthly	Yes
Oxford	14	Not ex officio	University (2) Boards of governors (4) R.H.B. (8)	Appointment by the 3 bodies without consultation	General purposes committee R.H.B	Quarterly	Yes
South Western	16	Not ex officio	Roy Coll. Physicians (4) Gen. practitioners (3) Roy Coll. Surgeons (4) Dentistry (1) Roy Coll Obst. & Gyn. (1) Coöpted (1 or 2) M.O.H (2)	Nomination by outside professional bodies	R.H.B.	Two-monthly	Yes and area committees
Welsh	39	Not ex officio	H.M.C medical committees (15) Mental health (1) Dentistry (1) Consultant advisers (16) Liverpool University (5) M.O.H. (1)	Nomination	R.H.B.	Biennially	Yes
North West Metropolitan	21	Yes	Regional consultants (6) Gen practitioners (2) Regl postgrad adviser (1)	Selection and nomination Nomination	R.H.B.	Monthly	Yes
South East Metropolitan	17	Yes	Gen. practitioner (1) Regional consultants (2) M.O.H (1) Teaching hospitals (1) Regl postgrad. adviser (1)	Nomination and selection Nomination	R.H.B.	Monthly or two-monthly	Yes
South West Metropolitan*	17	Yes and chn and vice-chn R.H.B.	Regional consultants (4) Medical schools (3) Regl postgrad adviser (1)	Nomination and selection	R.H.B.	Two-monthly	Yes

* The Western Area of the region has its own medical advisory committee.

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1. Brain, W R. *Lancet*, 1954 i, 1293
2. Lloyd Hughes T *Ibid* 1954 ii, 617

tive of either areas or specialties. Occasionally it includes the chairman and vice-chairman of the regional board, which shows that its essential function has been misconceived. Sometimes its value is lessened by the infrequency of its meetings.

Granted that some form of medical advisory committee to each regional hospital board is desirable, its exact constitution may well be determined by local conditions. It should represent the active clinical life, not only of the regional hospitals but also of the medical school (or schools) in the region. It should include representatives of the more important specialties; but, since it is impossible to include them all, specialist advisory subcommittees will still be needed. It should include some, but possibly not all, of the medical members of the regional hospital board, so that its policy is understood and supported in the board. Appointment should be by nomination, supplemented by cooption. Nomination by regional consultants' or area advisory committees will permit of adequate areal representation; cooption will be required to ensure adequate representation of the important specialties.

I am grateful to the senior administrative medical officers to the regional hospital boards, who provided the information I have summarised.

A VISIT TO KOLTUSHI

The Study of Conditioned Reflexes

RUSCOE CLARKE
M.B.E., F.R.C.S.
SURGEON, BIRMINGHAM ACCIDENT HOSPITAL

LEONARD CROME
M.C., M.R.C.P.E.
NEUROPATHOLOGIST, THE FOUNTAIN HOSPITAL, LONDON

WE had visited hospitals and laboratories during the previous ten days in Moscow and Leningrad, and talked, notebook in hand, to many doctors, all anxious to explain. Sooner or later there would be that odd conversation, begun with some remark such as this: "during the last few years we have tried to base our work on the teaching of Ivan Petrovich Pavlov." In some of the hospitals they then showed us conditioned reflex laboratories for animals and for patients. In others they had departments for sleep therapy. And in all they attempted to interpret such familiar states as hypertension or peptic ulcer in terms of Pavlovian physiology.

A few of us had read some Russian journals and were familiar with this new outlook; to all others it was disturbing and elusive. One thing was certain: Russian doctors spoke of it with conviction and enthusiasm.

Now we were on our way to the premier centre of this new science—Pavlov's laboratories at Koltushi. This "Capital of Conditioned Reflexes" was constructed in 1929 in celebration of Pavlov's 80th birthday, and the new 28 laboratories were then linked with 6 other institutes in Leningrad itself and with several clinics.

Fifteen miles out of the city we turned off the main road into a quiet country lane and were soon entering one of the Koltushi laboratory buildings, the former home of Pavlov. Like all the other houses in the village it was two-storeyed and vaguely Tudor—out of place in the Russian countryside. Was it an idea owed Pavlov to one of his visits to this country? The avenues and flower beds lay al deserted in the half-hearted September sunlight.

In the absence of the director, Academician Bikov, w were received by his deputy, Academician Airapet'yan Surrounded by pictures and simple personal memen of the founder, we were first given a general outline o the work of the institute and of the principles of Pavlovia physiology. The objective of their study, we were tol was an understanding of the functioning of the organi in its unity with the environment.

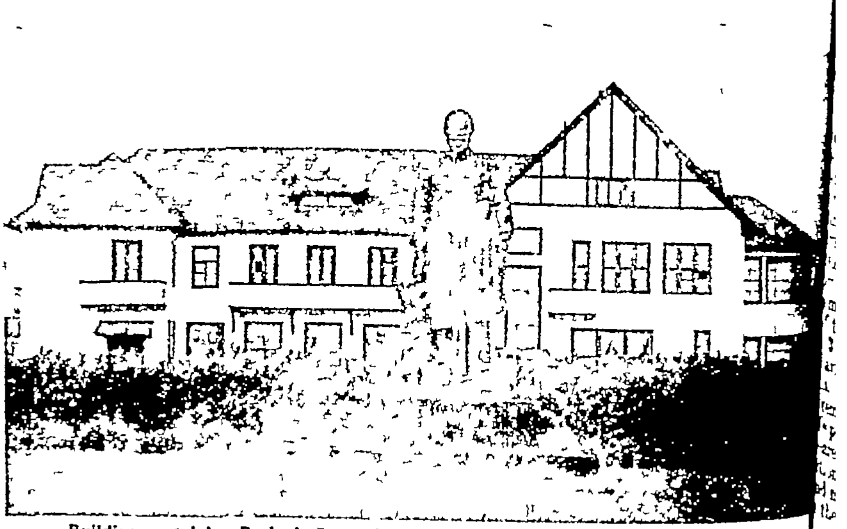
GENERAL PRINCIPLES

An animal, said our host, is in a state of consta interaction with its environment. Descartes knew alread that environmental factors determine the function of the organism by means of reflexes. Before Pavlov however, only inborn reflexes were studied. Man important discoveries had been made, especially by suc men as the great English physiologist Sherrington. B even Sherrington stopped short at the complexities o the brain, thinking that this was not amenable to stud by physiological methods. This domain was left t psychologists.

The way to a new approach was paved by the Russia physiologist Sechenov, whose *Reflexes of the Bra* appeared in 1862. Sechenov obtained experiment evidence that all the functions of the brain, includin mental activity, were also carried out by reflex actio But the question remained: How does it operate How is the interaction with the external environme achieved through the intervention of the brain? Pavlov great achievement was that he posed these questio correctly and discovered a new scientific method o investigation, objective rather than subjective, a metho that yielded more information than all the approache of the psychologists.

Pavlov found that, besides inborn reflexes, there ar others which arise from the individual experience of th animal. The basic inborn reactions may then be elicite in new ways and in new combinations by stimuli derive from the changing external environment. If any phenomenon capable of producing activity in a sensory pathwa immediately precedes, or coincides in time with, th operation of an inborn reflex, this new stimulus ca become capable of giving rise to the original inbor response. A dog is fed; a bell is rung at the same tim After a few combinations of the bell with the sight smell of food, the bell by itself calls forth salivation. An stimulus can act in this way and produce a reaction the animal.

How and where is the linkage formed? The answ was given by Pavlov not so much verbally as in thousand



Building containing Pavlov's flat and the Laboratory of Academician Airapet'yants of experiments Every stimulus capable of calling forth an unconditioned inborn reflex excites the unconditioned centres in the brain or lower parts of the nervous system at a level or levels determining the corresponding activity But every such excitation is also relayed to the cortex the highest and most recently acquired part of the brain Every external stimulus capable of giving rise to a conditioned reflex also excites the cerebral cortex—but somewhere else A state of excitation is in this way produced at the same or nearly the same time in two parts of the cortex and a linkage established between them This linkage is new and temporary but if repeated can become stable (Stable but not permanent This lack of permanence is a fundamental property of a conditioned reflex If the phenomenon which gave rise to it in the environment disappears or acquires a different meaning the conditioned reflex is altered or inhibited) Once it is established the unconditioned response can be obtained by excitation of the conditioned point of the cortex in the absence of the 'normal unconditioned stimulus A new reflex arc has been formed

These processes are precise, subject to laws, determined Thus any stimulus from the external environment if repeated in association with the stimulus appropriate to an inborn reflex can give rise to a new adaptive pattern of reaction These new reactions are formed in the cortex new conditioned reflexes allowing for the development of more intimately adaptive responses of the organism to the external environment Thus deciphered cortical activity can be defined as the processes involved in the relations between unconditioned and conditioned reflexes and also between the conditioned reflexes themselves In this way the animal becomes able to respond to an infinitely wider set of environmental agents than those which elicit inborn responses The concept is radical. There is nothing left of mental activity except complex relations between reflexes of one kind or another The mechanism of all mental activity is reflex Sechenov was right

Even such complex events as the whims of a child the romance of a girl the genius of Isaac Newton or of Garibaldi—all these are based on such reflexes Pavlov in his books *Twenty Years Experience* and the *Lectures on the Cerebral Hemispheres* gave precise experimental facts He founded a new science, a real science of behaviour the science of higher nervous activity Conscious and adaptive human behaviour depends on the activity of the cerebral cortex; but this activity is not only the mechanism of mental processes but also the dominant factor in the development of the individual

How are these processes localised in the central nervous system? Any approach to this question is based on three principles

1 No event can take place in the cerebral cortex without a cause immediate or distant in the environment There is no evidence for the occurrence of spontaneous cortical activity

2 Localisation must be related to the function of analysis and synthesis at the same time Pavlov demonstrated that the cortex may be regarded as a mosaic of analysers each of which has a centrally situated nucleus and very widely scattered peripheral elements. The finest analysis takes place only if the nucleus of an analyser is intact, while cruder analysis and much compensation for lost function after injury may be accomplished by the peripheral elements Synthesis—the formation of temporary linkages—cannot be localised to any one area of the cortex; it is taking place between all its parts

3 Localisation must be related to structure Here Pavlov opposed equally Lashley's theory of equipotentiality and the rigid mechanical concepts of localisation exemplified at present by the theories of John Fulton He preferred to think in terms of 'dynamic structures' areas concerned with a complex association of unconditioned and conditioned reflexes extending over variable and modifiable territory not only in the cortex but also in the subcortical centres He thought, in particular of the motor area of the cortex not as an effector organ for voluntary movement but as an analyser of kinaesthetic stimuli reaching it from all muscles of the body and in man especially from those in the hand and speech organs.

At Koltushi continued our guide, we have a great advantage in being able to undertake studies of the pathology of human disease alongside our experimental work on animals But the latter are essential for the knowledge of human activity A correct theory is essential and we believe that Pavlov's teaching provides the only correct theoretical approach to the study of functional relationships in animals and man It is vital for the clinicians who must learn that there is no such thing as disease in a single organ Every organ which is in any way diseased must in some way, to some degree affect the functions of the other organs and of the whole body The whole individual is ill, wherever the lesion is located the most important integration being achieved through the nervous system The central problem in medicine is concerned therefore with the functions of the nervous system with the elucidation of its laws of operation Naturally we do not exclude the study of other aspects of medicine and biology We attach importance to other forms of integration and interrelation, but we insist that the highest regulation of the animal is through the central nervous system and in higher animals, through the cerebral cortex

We asked if it was proved that the cortex alone was concerned with the formation of conditioned reflexes The answer was that where a cortex exists the highest regulation takes place at the cortical level but this does not mean that it can function without the lower levels of the brain and the nervous system It has been demonstrated that conditioned reflexes cannot be formed if the cortex is extirpated. Conditioned reflexes can however be formed in certain animals such as fishes, bees and silkworms, in which a cerebral cortex has never been developed In such animals it is the highest existing nervous ganglia which are concerned in the formation of conditioned reflexes

GENETICS OF HIGHER NERVOUS ACTIVITY

We then moved on to another building to meet Professor Feodorov and to hear and see a demonstration of his work on the inheritance of conditioned reflexes

Pavlov he said stated that conditioned reflexes must on a priori grounds be inheritable and become in the course of evolution inborn unconditioned reflexes During Pavlov's lifetime research had attempted to provide proof for this hypothesis but the experiments were not decisive and the results could be explained otherwise Recently work had been started again using mice because they could be rapidly taken through a number of generations A complicated piece of apparatus had been constructed wherein a mouse could be automatically released into a maze which if successfully negotiated led to a safe chamber The passages could be seen and the movements of the mouse recorded by means of a large wall mirror placed at an angle above the apparatus.

We sat and watched entranced the little white animals making their way with uncanny precision along the narrow corridors of this strangely fun fair like installation. The pathways were floored by a series of metal bars which could be electrified so that if the mouse remained too long en route to the safe chamber he would feel a continuous mild electric shock until the objective had been reached A bell or other neutral stimulus was set off and the mouse simultaneously released After six seconds the electric current was automatically switched in. After a few experiences of this arrangement a conditioned mouse would proceed straight to the safe cell on release and would avoid any shock at all.

The experiment could be made more complex by shining a light instead of ringing the bell and this time having the safe cell accessible only by a different route which made it necessary for the mouse to turn right instead of left if he were to reach the safe area before the current was switched on It was possible to continue conditioning experiments so that the mouse would choose the correct path when the left and right routes were alternately opened with the same stimulus Thus varying degrees of complexity in the conditioning process could be developed in a precise way

All the conditions of this experiment allowed for its operation without any intervention by the experimenter other than pre selection of the relation between the electric current, the pathway leading home, and the indifferent stimulus applied

With this technique a group of animals was divided into two groups, one a control The experimental group was trained to a given degree of complex conditioning and then allowed to breed as were the controls Each generation of the non controls was submitted to the same training process After a certain number of generations the controls were tested for their ability to acquire more rapidly conditioned reflexes necessary to avoid the electric shocks, and thus compared with similar mice whose parents had been trained

We were told that during the last few years this experiment had yielded decisive results, but that further experiments would be continued with a variety of other animals It was freely admitted here that what had been in fact acquired were not particular conditioned reflexes but the capacity to form them in conditions of a persistent change in the environment calling for these reflexes

These experiments are reminiscent, of course, of the work of McDougall and of Tryon and appeared to us to be of fundamental importance It is with great interest that one awaits their publication and repetition elsewhere This work is, incidentally, to be associated with studies of the minute structure of the brains of these animals, in an attempt to gain evidence of structural change associated with this evolutionary process which is thus being achieved in the laboratory

COMPARATIVE PHYSIOLOGY

We moved on through the trees to the next laboratory for a demonstration of work on the comparative physiology of higher nervous activity

The problem here was adaptation of young animals Previously, we were told, many of the adaptation processes had been regarded as entirely dependent on the active rôle of the mother, with the young animal behaving more or less passively It "contemplated" but did not adapt This conception was considered improbable on theoretical grounds, but the problem of demonstrating the acquisition of conditioned reflexes in the newborn animal was difficult technically Pavlov's salivation techniques were inapplicable and new methods had to be developed to suit different species of animals

Experiments with puppies showed that conditioned reflexes could be formed in relation to the sense of smell immediately after birth

Two days before parturition the bitch was specially cleansed and treated with a scent Puppies taken away at birth would respond by withdrawal on presentation of a piece of cloth steeped in the scent But after one experience of suckling, for even as little as five seconds, they would subsequently, when hungry, crawl towards the scented cloth, whining and behaving as they would normally towards their mother With a different smell the response was totally negative, they turned their heads away and crawled back Even premature animals showed this capacity for acquiring conditioned reflexes and were quite helpless if deprived of this capacity by division of the olfactory pathway They were then unable to suckle when put to their mother and would starve unless given a great deal of assistance in feeding

The first important analyser in the life of a puppy is that of smell

By the fourth day puppies respond to adequate auditory stimuli, and by the fifteenth day conditioned es can be established to sound

A bitch is kept in one cage, the puppies in another bitch is allowed to visit the puppies, but this is accom by sound After two or three combinations of sounds the mother's visit the puppies will respond to sound as if the mother were approaching

Similar types of experiment using the visual analy showed that conditioned reflexes could be established 25–30 days Further experiments studied the estab ment of conditioned reflexes through the vestib apparatus

Birth took place in a box on springs the vibrations of wh could be recorded The puppies could be conditioned to re to any movement of the box as to their mother's approa If born in a non moving box puppies would not respond such movement These conditioned reflexes could be obtain by the twelfth day

Further experiments of this kind were concerned w the problem of types of higher nervous activity Pavlo detailed studies of the reactions of animals had led h to appreciate the significance of differences in t response of different animals to attempts to indu conditioned reflexes He found among his animals do with strong nervous systems and with weak ones T strong ones could be further subdivided into balanc (phlegmatic) and non balanced (choleric) From t viewpoint of the mobility of the nervous processes t strong balanced animals could be either mobile (sangui or inert It will be seen that this classification resembl the Hippocratic one of human temperaments, the we dogs suggesting the melancholic temperament Expe ments have been now pursued in this laboratory with t object of creating and changing such types

Experiments were begun as soon as the dog could leave mother Some were given the maximum free contact w their environment, others of the same litters were to so extent isolated These changes were associated with delib ately varied diets Different types of higher nervous activ could be deliberately produced in this way, and, in early sta of life, changed in a desired direction In fully grown do it has been found, the basic properties of the nervous syst are almost impossible to change, though existing quali can be enhanced or moderated

The experimental production of types has been link with the study of the emergence of the various sens analysers A current experiment was dealing with relation between *subliminal* painful stimuli and effects of stimulation of the auditory analysers

Litters of puppies were divided into three groups C group was fed while rattles were sounded, a second group subjected to the rattles plus subliminal painful elect stimuli, a third acted as controls This was continued six months with careful observation of behaviour during t period The puppies in the second group developed slowly passive defensive reaction behaving as though they we frightened The first group and the controls developed such reaction

After six months they were all given Pavlovian saliva fistulas so that their salivary secretion could be used as indicator of the production of conditioned reflexes The do which had been subjected to the rattles plus the pain stimuli formed no conditioned reflexes, their cortex seem to be in a permanent state of negative induction—inhibit The dogs subjected to the rattle treatment only were str and highly reactive—more so, indeed, than the controls. addition, the inhibited animals did not grow well and beca bald *Attempts were made subsequently to cure them* by complete change of environment In some of them this co be done, but others remained permanently abnormal.

Another point of interest in relation to the rea of the organism to infection was that it had been that a leucocytosis could be produced as a cond reflex

BIOCHEMISTRY

In another laboratory we discussed the contri biochemistry to the Koltushi research on condit flexes. Pavlov had envisaged that in course of time he complexities of the brain structure—its microscopic orphology—would be related to the processes under ing the formation and interaction of conditioned flexes and that biochemistry would throw light on the molecular nature of the processes involved in nervous ctivity Biochemical research had, however, lagged ehind

An approach was now being made to the basic processes underlying cerebral activity Already it had merged, for example, that the cortical processes of the og and the rabbit are biochemically very different gain, whereas it was previously thought that the white matter of the brain, consisting largely of connecting bres is essentially passive in a functional sense, it has een found that biochemically the white matter is often more active than the grey The task is to extend our iological knowledge of nervous processes and particuarly of those underlying the development and interaction f conditioned reflexes in the cortex Histochemical methods were showing for example, that the distribution f nucleic acid in the nerve-cells differed with different unctional states—with excitation and inhibition, both onditioned and unconditioned

CORTICO VISCERAL RELATIONSHIP

Regretting the absence of a biochemist amongst us, e proceeded to the next laboratory—of Academician irapet'yants, our host and guide He wished to tell us omething of the studies on cortico visceral relationships n which he had been working with Academician Bikov ut thought we had had a long morning and were perhaps ired We asked him how long he would take to tell us f the work. He said that it could be done perhaps, in three hours, or three days or three weeks, or three years ut he would tell us a little in twenty minutes and then here would be time for questions. We agreed

Bikov was one of Pavlov's pupils and has been engaged n this work for the last twenty years It was necessary o show experimentally that the cerebral cortex really ontrols without exception all functions of the body, nd that conditioned reflexes can be developed in connection with all functions of the organism It has in fact een possible to establish conditioned reflexes using a arge variety of bodily functions—secretion of bile, ecretion of urine, intestinal peristalsis, and vascular eactions All reactions which can appear as a result of ppropriate stimuli as unconditioned reflexes can be voked by any indifferent stimulus which coincides in ime

Ingestion of a lot of water will result in diuresis. If his drinking is accompanied by the ringing of a bell hen later the bell alone will evoke diuresis Excitation preads along a cortical path which has now been established and the kidney is brought into operation If such hings can happen in ordinary life they can also happen under pathological conditions Pathological processes an never take place without involving in some way the erebral cortex The pathological state of an organ does ot necessarily originate in the cortex although it may o so but the cortex always plays a part in the development or arrest of any pathological processes

What is important here is to take the argument a stage urther If the cortex controls and regulates internal organs is it in its turn influenced by them ? If we can orm conditioned reflexes to external stimuli, can conditioned reflexes be likewise formed by 'indifferent " stimuli arising within the body ? To answer these questions has been the particular task of Airapet'yants s boratory

Let us take for example a dog with a gastric and a livary fistula You introduce some water or a balloon to the stomach carefully so as not to affect other sense gans No saliva will be produced from the salivary fistula Now you combine gentle gastric dilatation with feeding After a few combinations the gastric dilatation alone will stimulate the flow of saliva A full stomach has begun to stimulate appetite !

From this and similar experiments with other organs it is concluded that the stimulation of any organ, of threshold intensity, leads to excitation of the cortex. If this is accompanied by excitation of another cortical area by a stimulus derived from another organ there is, as with external stimuli, a linkage a conditioned reflex can be established The cortex is capable of responding to stimuli from all somatic organs and viscera—mechanical chemical and physical—by analysis and synthesis, by the development of conditioned reflexes It can react to degrees of temperature, concentration of chemical substances and chemical differences As with the external environment so all reactions of the internal environment operate through reflexes and these too include conditioned reflexes All this should not be interpreted, however, in the sense that processes in organs can be primary ' or ' spontaneous They do not occur without a cause in the environment, either immediate or more remote

This we were told is not only of importance to theory and to philosophy but also to clinical medicine. On a-priori grounds it may be assumed that the human organism like that of animals operates through such reflexes but it is also necessary to observe this in man We need proof and detailed understanding of the mechanisms The operation of the brain is, moreover more complex in man because he possesses a second signalling system (The discovery that words operate as conditioned signals of a second order was one of the most remarkable chapters in the work of Pavlov Towards the end of his life he came to grips with one of the most mysterious problems of cerebral function—the nature of human thought He found that it was intimately related to speech This in its turn was mediated by conditioned reflexes of a more complex character constituting an additional signalling system capable of greater adaptability to a much wider range of environmental influences —making possible indeed such processes as ' abstract thought ')

In the final stages of our visit we discussed some clinical experiments which showed that changes in visceral function can be produced by previously indifferent stimuli bringing into action special associations which have been formed with words and figures In patients with peptic ulcer for instance, contractions of the stomach are associated with sensation of pain By a process of conditioning, the figures on a clock could be made to produce both contraction of the stomach and the pains of an ulcer Thus we were shown something of the experimental basis for sleep therapy in certain diseases one of the effects of which is to exclude the harmful action of a whole range of environmental stimuli which have become associated with pathological processes

CONCLUSION

It was time to leave We wandered out into the open and looked at the growing village with its new laboratories and homes for those who work in the laboratories We saw some special rooms for the more complicated experiments on dogs and apes. They are designed to eliminate accidental features and the impact of the observer on the experiment (We had seen on other occasions how fond the physiologists were of playing happily with their experimental animals " after hours ") The rooms are elaborate and sound proof Mechanical contrivances present the dog with a plate of food on the pressing of a button Innumerable controls operate a wide range of stimuli Special recording devices register changes in the secretion of the saliva and of other visceral functions There were other simpler fixtures designed for use in any laboratory undertaking work on conditioned reflexes

We shook hands and exchanged compliments Half an hour later we were threading our way cautiously past ruts and pot holes in the as yet unfinished streets of the advancing Leningrad outskirts It was three or four hours that we spent at Koltushi, and we had no more than a glimpse of the new science Was it a glimpse into the future ?

PREVENTION AND MENTAL HEALTH

Conference of the National Association for Mental Health

OPINIONS differ about the possibility, in the present state of our knowledge, of preventing mental ill health , but there is a general feeling abroad that in time research will bring enlightenment about this and many other aspects of mental health work At this year's annual conference of the National Association for Mental Health, held at the London County Hall on March 24–25, with Mr KENNETH ROBINSON, M P, presiding, Mr IAIN MACLEOD, the Minister of Health, opened the first session

OPPORTUNITIES IN THE HEALTH AND EDUCATION SERVICES

Mr MACLEOD spoke of the fears and prejudices about mental illness which still hinder both the use made of the mental hospitals and the recruitment of nurses General practitioners and voluntary workers, who can do much to educate the public, should be well informed about recent advances in the mental field Mental hospitals are arranging open days and forming leagues of friends , and the press and the British Broadcasting Corporation are helping greatly in spreading information Probably all mental disorders are of multiple origin, but it seems clear that in their prevention we must go back to old wisdom recognising that lack of love, lack of companionship, and lack of security are potent causes of breakdown There are now 650 outpatient clinics in the country for adults and children who need treatment On the preventive side, local authorities have the power to provide community services , but though they undertake various types of work which may be called preventive, they have been slow in developing a formal pattern Their opportunities for preventive work among children—through the health visitors and the maternity and child-welfare clinics—are very great Health visitors, indeed, are taking an increasing interest in the subject , and a working party is now considering how their training should be revised and widened He had, he said, asked the local authorities, last November, to do all they could to prevent the break up of families Once a child leaves school he has no routine public health supervision , hence it is important that his family doctor should be in full touch with local authority services, so that he can call on them when necessary It is not yet possible to advise local authorities, by circular, on what mental health services they ought to provide, but they are being urged to take a keen interest in this work Public education will gain momentum as patients and their relatives get a new awareness of mental hospitals and their services Mental hospital buildings are expanding under the new programme and with better buildings we can look forward to attracting more recruits to nursing

Dr F A E CREW, F R S , professor of public health and social medicine in Edinburgh University, said that medical knowledge has so far contributed little to the prevention of mental illness He sees no real hope of a speedy solution to this problem, but thinks that social, as opposed to individual, studies provide some clues

A Chicago survey of mental hospital patients suggests that not only mental illness but social factors such as poverty, crime and suicide, are related to a particular factor—namely, 'isolation' This finding is supported by experience York, that mental illness is commoner among immigrants than among the native born population among the children of immigrants than among native- children The newcomers, until they are absorbed fully the new culture, are lonely and isolated A study, in London boroughs, has shown a negative correlation of su with poverty, but a positive correlation with loneli Other investigations, in Massachusetts and in Norway, h shown that the chances of admission to mental hospital greater for the unmarried, widowed, or divorced, particul men, than for the married Either those who marry, Prof Crew said, are less liable to mental illness than those remain single, or else marriage is protective He ment also a study, not yet published, made in Edinburgh Dr Donald Cameron, of the places of origin of mental hos patients He found that the admission rate of those the Highlands and from foreign countries (which did include England and Wales) was higher than that of Edinburgh born , and that among the patients the s were twice as numerous as the married

Such findings, Professor Crew went on, cannot be f interpreted without more study What is marriage? this country a reasonable prerequisite for the foun of a family, that microcosm in which children mature , an opportunity for emotional and se security , and also, in the lovely phrase of the Pr Book, "for the mutual society, help and comfort the one ought have of the other" The married pe is no longer alone but a member of a group with b of affection, and with a place of his own and thing his own—a refuge This may determine whether or he goes into a mental hospital, and if he does how he stays there Our society has produced condit which are to a greater or less extent intolerable there are many bewildered and perplexed people wit a purpose During the war the mental health of country was surprisingly good the lonely were res —there was a place and function for all The ca of mental ill health are partly individual and pa environmental , and while it is desirable to plan f society in which causes of mental ill health are remo we need to know much more before we can create a society At present we can only attempt to stem torrent

The rise in the admission rate to mental hospita not trustworthy evidence of an increase in me ill health, because patients are now going in volunta hopefully, for treatment But the incidence may rising, and that may be either because our stoc deteriorating or because the circumstances of life inc ingly provoke mental illness We must find out wh We cannot be mistaken, however, in attempting remove those provoking causes which we know important for mental health that the individual sh be attached to a faith, a cause, a purpose, which gi serenity We talk of mental health without know what we are talking about , but if it is peace wit and peace within the environment, it is perhaps a ma of philosophy rather than the ticking of a mach What a man does should be within his competence value, and regarded as valuable by others He m not feel he is an outcast but a part of a group , must take into marriage an understanding of what involves, and know something of his own sexual natu (For the young person, Professor Crew remarked passing, a motor bike is no substitute for a cage of m

During the war, the Navy and the Royal Air Fo had the more intelligent recruits , the Army got all t dull, the neurotic, and the unstable It is no lon true that the dull man makes the best soldier he ne today, average intelligence and not a little techn skill The duller men in the Army were apt to bec maladjusted and neurotic absentees In the Pion Corps, however, there were some men too intelligent to have been sent there, and they too became neuro they benefited by being given more responsible No man should be employed in work either above low his mental capacity Doctors, instead of signing rtificates saying a man is not fit for his job should rhaps start signing some which say 'Job not fit r man We are dedicated Professor Crew concluded the creation of an environment optimal for human This is a cause which can claim our unrestrained otion and one from which we can hope to derive ding joy

RACTICAL PROBLEMS IN LOCAL AUTHORITY SERVICES

In opening what the CHAIRMAN described as a rumbles session Dr J L BURN, medical officer of lth for Salford offered as his first grumble the lack recognition of the importance of mental health in al authority schemes. They spend far less on it than their other health services and place too much phasis on the mental hospital and too little on the me 'Only when other public health resources (such rehousing) fail he said do we think of mental re' and this is an expensive way of arriving at a agnosis. Many opportunities of preventing ill health uld be taken with little expenditure The antenatal nics could be used more freely *for teaching the club* ea could be extended group therapy *encouraged some* mily doctors might be persuaded to send patients rlier for treatment, hostels could be provided for mental fectives, and educationally subnormal children (who ovide a high proportion of delinquents) could be pervised for three years after leaving school The eak up of a family often dates from their eviction for n payment of rent: there are no statutory funds to de them over such a crisis (though health visitors often nd what is necessary out of their own pockets) He rged the need for 'more bridges'—such as case nferences between hospital and local authority staffs efore a patient leaves a mental hospital

MISS E STEPHENSON chief nursing officer at Newcastle pon Tyne as a nurse midwife and health visitor, has ood opportunities for observing the barriers our services uild up between each other (Some of them, she said re themselves suffering from mental ill health they eed to foster good family relationships within their ome departments) In the home the family doctor the ealth visitor the midwife and the district nurse are ll preventing mental ill health by being good listeners is part of the health visitor's job in addition to teach ood living but she needs to know when to call in an pert and to have an expert at hand to call in She o since she knows the family ought to be invited to tend case-conferences.

Miss S FRIEDMANN educational psychologist to the ity of Oxford regretted that local authorities have so *ttle sense* of urgency about mental health work They ould never dream she said of appointing one dentist r one afternoon a week to look after the teeth of a opulation of 10 000 children but they often appoint ly one psychiatrist to such a population—though ental growing pains are just as common as toothache he child guidance clinics have enormous waiting lists ad children may wait a few weeks or a few years for eatment—which should be given early and neither late *or* as a last resort

Mrs. M ORMEROD chairman of the joint Bethlem oyal and Maudsley Hospital board of governors and ember of the London County Council health committee id that the grumbling of the experts had fairly and uarely exposed the faults of the local authorities She she said, a reasonably good mother but whenever she terviews a nicely dressed woman with two clean and eely dressed children and learns that they and the ther are living in one room—eating sleeping and doing e family washing in it—she wonders what sort of *mess* e would have made of a like job Something can be ne by education committees and fortunately Lon ners like spending money on education She thinks that every penny spent on child guidance and on classes for the educationally subnormal child is well invested helping to prevent both mental ill health and crime But housing of course is a more difficult matter She spoke of the closer coöperation of the psychiatrist and the family doctor which has been achieved in Amsterdam The Maudsley Hospital she said *is hoping to start a* domiciliary service with a view to keeping more patients in their own homes for treatment We have some glimmer of how to make people secure we know security is based on happy family life Sir Geoffrey Vickers[1] has described the most important promise of mental science as that of "helping us to conceive of mental health as a positive dynamic condition of mind to see the path towards it to develop the will to achieve it' "We members of local authorities' Mrs Ormerod said must develop the will to achieve it

PROMOTING MENTAL HEALTH IN A LOCAL COMMUNITY

Dr S A MACKEITH consultant psychiatrist to a group of Norfolk hospitals pointed out that local authorities are desperately short of psychiatrists and psychiatric workers, whereas regional hospital boards though they have not enough of these workers do nevertheless employ considerable numbers of them He suggested that the boards should permit and indeed encourage their psychiatrists to devote one session a week of their time to mental health work for a local *authority—not* in fresh treatment clinics but in preventive mental health fields found by experience to be fruitful, He himself had asked the medical officer of health of a local *authority* to allow him to work for one session a week in a maternity and child welfare clinic where he hopes to learn in time how to spot at an early stage the over anxious or otherwise disturbed mother who will be *bringing her child* to a child guidance clinic in 5–10 years time An experienced psychiatrist working part *time for a local* authority might help in various ways—by holding discussion sessions for midwives and health visitors attending meetings of the medical officers employed by the authority, and acting as psychiatric adviser to the M O H and psychiatric catalyst to the medical work *of the* local authority generally The training of duly authorised officers he thinks should be weighted on the social rather than the psychiatric side but *nevertheless* they should have some training in psychiatric case work This should be given by psychiatric *social* workers, who like the regional board s psychiatrists should be encouraged to give a little time each week to the local authorities. They should be asked especially, *to advise* at reception-observation centres for children

He mentioned the Amsterdam scheme,[2] in which the psychiatrist, before recommending any treatment interviews the patient in his own home Other experiments deserving wider study are the day hospital and the night hospital (from which patients go out to work) Psychiatrists might also help local authorities by advising on the appropriate treatment of old people with mental disorders. We are still too ill informed about prevention to be dogmatic but one important thing is to respect the point of view of the other *fellow* Let us not rush to tell other people how wrong they are in what they are doing' He believes in supporting the *authority* of the family and increasing its self-confidence—particularly the self-confidence of the young mother in her *feelings* and impulses toward her child. Whatever we do growing up from infancy will always be a strenuous and frustrating business adolescence a stormy time and no *amount* of tactfully given information about the facts of life will alter that Perhaps good mental health like good morale in an army unit cannot be achieved by direct means perhaps it is he said "the bloom on the fruit of a really sound society"

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[1] *Lancet* March 12 1955 p 521

[2] See Ling T M *Ibid*, 1954 i 112; *ibid* p 111

In England Now

A Running Commentary by Peripatetic Correspondents

ONCE in the days of our master, the Commander of the Faithful, Haroun El Rashid, on him be peace, in the season of the ripened dates, there came two wise men riding from the west And after they had shaken off the dust of the plains they sought the ear of the Caliph But Abu Newas, his wazir, stopped them at the gate of the City of Peace and said What manner of news do you bring from the Land of the Free? And the first wise man said Lo, we bear a magic potion for your maidens and your young men, that they may smile upon each other with pearls as white as asses' milk in the moonlight That your wives shall not spit their teeth into the dust when they are heavy with child That your aged ones shall not chatter false mouthings in the market place And Abu Newas was glad in his heart, for he found joy in both the comeliness of maidens and the flesh of a roasted sheep

So the wise men were led into the presence of the Caliph And Haroun El Rashid heard their say And Abu Newas whispered Give them a thousand dinars, O master, for they worship gold in their land, and let us have neither holes in our teeth nor pains in the night But the Commander of the Faithful said Stay! I would first know how this magic potion, which you call Fluor, shall be given to my people And the first wise man replied It shall be poured into every well in your kingdom, that all must partake of the blessings of mankind But Haroun doubted and said How shall I know that it will not harm my people if they drink too much? And the second wise man replied Their teeth will become mottled as the camel's and their backs as stiff as rocks, but see, we have a thousand scrolls in our caravan to bear witness to the wisdom of our wise men And Abu Newas whispered Their people worship a god called Science only a little less than gold Let us test their magic on thirty-six of our children And Haroun said Let it be so

But many moons passed, and Abu Newas had to slip with the cunning of a jackal through the time of Questions Some of the thirty and six children were changed by magic into men and women, and the scrolls were lost in the secret registry And Abu Newas cried three times that the wise men of the west must be wiser than any tests But the Commander of the Faithful was beleaguered by his wives, who made much song and dance, and said It is against the will of Allah to medicate the masses It is not justice to make your people of all ages drink this Fluor when even the wise men say its magic spell works feebly after eight summers have passed away And yet other zealots trailed strange western fish called herrings across the palace yard And the Commander of the Faithful held his head and groaned Bring me a goatskin of wine, and cast this noisy mob into the river that they may take their fill of water And cast Abu Newas and the wise men in as well, so that once more I may rule over the City of Peace Let it be so

* * *

It's the nights that get me down A typical night in our family goes like this Midnight, I've just got warm and am dropping off when banshee wailing from Second Child recalls me. I get up, find my slippers and dressing-gown, and stagger down the arctic stairs to get him a drink (warm orange, in pink mug—no other acceptable) and deal with his other metabolic needs Then, cursing roundly, I tuck him up and go back to bed, to find my husband hogging my warm patch and snoring heavily A few sharp kicks right this, and I settle down and am deliciously warm and sleepy when agonising howls from Third Child break out. Same procedure as before She is starving and soaking I apply her drink (warm milk in a red mug) to the appropriate end and dry towelling to the other, fling her back in her cot, and stamp off to bed again This time I manage to snatch a little sleep, and it is 3 A.M. before First Child has a nightmare, and eldritch screams of "Mummy, Mummy—there's a fire engine in my bed!" be dealt with (He has cold blackcurrant in a blue mug) The cat is now in my warm place
the morning my husband asks brightly, "Well—w
sort of a night did you have ?"

* * *

Professor A decided to telephone Professor B to
they could go to a committee meeting together Pro
A is a busy man and he cannot be expected to hold on
a telephone line while the nurses look for Professor
So he has a secretary to whom he says "Get me
fessor B on the phone" Professor B is equally busy
he cannot be expected to answer the telephone himsel
or to hold the line while someone's secretary says "W
you hold the line, Professor A would like to talk to you
So Professor B also has a secretary who answers h
telephone and puts through his calls

When Professor A's secretary asked Professor B
secretary if Professor A could speak to Professor
Professor B's secretary felt some alarm It appea
that on a previous occasion when Professor A h
telephoned Professor B, Professor B's secretary had go
to a great deal of trouble to find Professor B, who w
in the middle of a ward round at the time with some
or 20 lesser beings following him Unfortunately wh
he got to the telephone Professor A's secretary w
unable to find Professor A With great presence of mi
she had said that Professor A had been called aw
suddenly, but Professor B did not believe this st
—and indeed he was quite right, since Professor A w
known to be rather forgetful and had actually gone
to the laboratory to look at some kymograph tracin
Professor B's secretary therefore produced a gene
solution to all problems of this nature, she simp
announced that Professor B was engaged at the mom
and that he would telephone Professor A when
was free

Those who have the gift of seeing general princip
behind the ordinary details of everyday life will at o
grasp the fact that this story shows up a fundamen
problem which we might call "the law of telepho
precedence" Stated as simply as possible it imp
that a great man shall not be made to give way t
lesser man in answering telephone calls One difficu
remains—that of establishing rules for settling pr
dence And here I think we are entitled to some h
from the National Health Service Many secreta
lacking in experience would be greatly helped if they
some system of finding out a man's importance quic
What about a simple scoring system? 10 marks
a consultant or a professor, 8 for an F R C P, 6 for
F R C S or an M R.C O G, 4 for lesser qualifications
D P M., M D, or F R S Hospital appointments on
medical staff would range from 7 to 2 and there are so
delightful possibilities involving very small fractions w
irrational solutions for non-medical supervisors
administrators Anyone in receipt of a merit aw
takes top priority

* * *

I was new to general practice, and Social Medicine h
loomed large in my training When I came across
first example of gross overcrowding I wrote a stiff let
to the housing authority They fell for the story a
Mrs W was offered a house on the new housing esta
On Friday evening she came to the surgery to thank m
She and her family of four would exchange their o
room for six the next day

On Saturday morning Mrs McG came to add h
family of five to my medical list She had moved in
Mrs W's room "And could I have a letter for th
housing like you gave Mrs W?"

* * *

The old man in my outpatient clinic complained o
indigestion, but seemed unable to give me a cohere
account of his symptoms Eventually in desperation
asked him how he knew he had indigestion. He brightene
at once "The X-ray showed a septic cat in m
duodenum" In astonishment I said "A septic cat"
"Yes," he replied "a septic cat I don't know wh
they meant, but that's what they said, a septic c
They've been treating it with milk."

* * *

Is it true, or is it a rumour, that the manufacturers
dexamphetamine are living on the fat of the land?

Letters to the Editor

MUSCULAR DYSTROPHY

SIR,—The Central Council for the Care of Cripples has decided to form a Group or Association of patients suffering from Muscular Dystrophy, and has already found that there is considerable interest in such a development, particularly among the patients and their parents. Numerically the problem is not a large one but the people concerned are often isolated and it is the Central Council's intention to establish a friendly link, to provide interest and amusement for the children and to distribute leaflets of general information to parents, members and others.

It is beyond dispute that research is of paramount importance and your readers will agree we feel, that there can be no firmer basis on which to develop the work which is contemplated than through the advice and support of the many distinguished neurologists and other specialists who have accepted appointment to the Medical Advisory Committee which the Council has set up.

The chief difficulty from the Central Council's point of view as a voluntary society is to find the people it wishes to help. Nevertheless ascertainment of the extent of the problem is an essential if real progress is to be made. I am therefore writing to ask anyone in sympathy with this movement to put their patients or others known to them in touch with the Central Council for the Care of Cripples. I must emphasise that the Group will remain within the ægis of the Council which intends to use its existing County Associations rather than to superimpose a new organisation.

Central Council for the Care of Cripples
34 Eccleston Square
London, S.W.1

HARRY PLATT
President
Muscular Dystrophy Group

HALLUCINOGENIC DRUGS

SIR,—We hope you will allow us to voice a word of warning regarding the use of the so-called 'hallucinogenic' drugs, notably lysergic acid diethylamide (LSD 25). Although its application especially as an adjuvant to psychotherapy is suggested by recent work[1,2] we feel that too little as yet is known about individual differences in susceptibility to warrant its use except under closest supervision. Our own observations in normal volunteers, and reliable reports from colleagues suggest that:

1. During acute intoxication the subject may potentially be a danger to himself and to others.
2. In single instances a delayed and exceptionally severe response may take place and be followed by serious after-effects lasting several days.
3. Early psychotic conditions may be aggravated by the drug.

Until more is known about its mode of action, we urge those interested to refrain from using the drug in out-patients or in day hospital patients and restrict its use to inpatients—and then only when constant supervision by trained personnel is available. At this early stage it seems to us wise to tread cautiously and to protect what may be a promising new method from indiscriminate use and untimely haste.

Department of Experimental Psychiatry
University of Birmingham

C. ELKES
J. ELKES
W. MAYER GROSS

BURNS FROM ELECTRIC BLANKET

SIR,—An unusual domestic hazard which may face young children was recently illustrated in my practice.

A 4-year-old boy was sleeping in his parents' bed, in which an electric blanket had been placed beneath the lower sheet. The heat control had previously been set to the minimum. The mother found the child unconscious and rigid; the father in attempting to rouse him received a not inconsiderable electric shock from the boy's body. The blanket having been disconnected the sheet was found to be saturated with urine and the child had suffered full-thickness burns of the skin of his back, buttocks and thighs. He rapidly recovered consciousness and was admitted as an emergency to the nearest hospital. Subsequently he was transferred to a pædiatric burns unit.

Since the use of electric blankets is becoming increasingly widespread both in homes and in hospitals, the dangers of their use by infants, young children and enuretics should surely be stressed. Moreover it should be incumbent on manufacturers to make provision for adequate earthing and preferably to fit an automatic cut-out to counter an accidental short circuit.

London, N.11

NEVILLE DAVIS

JOURNEY'S END

SIR,—A year ago in an article entitled 'African Journey'[1] I recorded some impressions of a trip from Cape Town to Cairo during which I visited the main medical centres in the Union of South Africa, Southern Rhodesia, British East Africa and the Sudan. From evidence obtained at many clinicopathological conferences I came to the conclusion that certain diseases, which cause a vast amount of ill health in Europeans are much rarer in Africans. They fall into two main groups:

(1) Diseases which are commonly called 'psychosomatic' by those who believe that emotional factors are of major ætiological importance—e.g., peptic ulcer, essential hypertension, rheumatoid arthritis, and toxic goitre.

(2) Diseases which may be caused by metabolic factors—e.g., atheroma and its sequelæ (cerebral thrombosis, coronary thrombosis, and peripheral vascular disease), cholecystitis and gall-stones, and diabetes.

This difference in prevalence could be attributable to racial and constitutional factors or to environmental factors such as diet, housing, and associated infections. In concluding my article I suggested that if the diseases which are commoner in Europeans than in Africans are due to environment rather than race their prevalence should be conspicuously higher among those Africans who have adopted Western customs, eat Western food, and are submitted to the emotional strains of modern civilisation. To complete my African Journey therefore, I went last December to the Southern States of the United States of America so as to obtain information about the prevalence of these diseases in the American Negro.

When I previously visited South Carolina and Georgia thirty-two years ago the economic, social, and educational state of the vast majority of coloured people was exceedingly poor. Malnutrition was rampant, housing conditions were usually deplorable, and the daily wage was often as low as 50–75 cents. Two world wars and the industrialisation of the Southern States which has resulted from them have led to a revolution in the living conditions of the Negro.

Alike in the factory and in the field he receives the same rate of pay as his white neighbour (perhaps 6–12 dollars a day). A Negro woman doing domestic work is paid 6 dollars a day. Negro boys and girls go to well-constructed primary and secondary schools and many proceed thereafter to college. The average coloured family lives in a house which, though the general standard has greatly improved, would still be considered unsatisfactory by white people of the same economic class; but with less to pay in rent and taxes for his house the Negro may have more money than a white workman, *on the same weekly wage*, to spend on food, drink, tobacco, motor cars, and other luxuries.

Standing in a main street in Charleston, South Carolina, ~~one evening I watched the stream of cars which carried the~~

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[1] Sandison, R. A., Spencer, A. M., Whitelaw, J. D. A. *J. ment. Sci.* 1954, 100, 491.

[2] Sandison, R. A. *Ibid*, p. 508.

[1] *Lancet*, 1954, i, 614.

workers back to their homes in the suburbs and in the surrounding country There appeared to be more cars driven by coloured people than by white people, while the condition, make, and size of the cars seemed to be the same in the two group

In one generation the material prosperity of the American Negro has been transformed, and at the same time malnutrition and deficiency diseases (such as pellagra) have virtually disappeared, malaria has been eradicated, and many diseases such as enteric fever and dysentery, which are associated with bad hygienic conditions, have been greatly reduced On the other hand, material prosperity does seem to have been bought at a considerable price, for everyone with whom I discussed this matter told me that the psychosomatic and metabolic diseases have much increased among the Negro population of the United States Dr V P Sydenstricker, professor of medicine in the University of Georgia, informed me that whereas at the beginning of his professional career forty years ago these diseases were rare among Negroes, they are now very common Several distinguished physicians told me, indeed, that Negroes are now developing malignant hypertension and the collagen disorders more severely and at an earlier age than white people

The evidence before us leaves little doubt that the origin of many diseases is closely related to the working and living conditions and eating habits of Western civilisation The relative importance of metabolic and emotional factors in the ætiology of these diseases remains to be ascertained We are also left with the question whether people who have once enjoyed the material pleasures of modern times will ever be willing to return to a simple agrarian life

Edinburgh STANLEY DAVIDSON

INVESTIGATION OF METABOLIC DISORDERS

SIR,—My colleagues and I are investigating the population genetics of three rather rare metabolic disorders pentosuria, cystinuria, and alkaptonuria We should be very grateful if general practitioners and consultants could put us in touch with patients known to have any of these disorders

Department of Biochemistry
London Hospital Medical College,
Turner Street, London E 1 H HARRIS

AIR EMBOLISM

SIR,—Dr Snell (March 19) rightly says that lowering the head as a first aid measure may be life saving in this emergency and adds, but does not stress, "preferably with rotation to the left side" He speaks of "pleural shock" and "obstetric shock" together as if, when due to air embolism, they were of the same kind, whereas the former is arterial and the latter (primarily) venous

In arterial air embolism such as may cause "pleural shock" in artificial pneumothorax therapy, air can reach the brain and cause many, often transient, symptoms, but it can also enter the right coronary artery and kill the patient quickly In the left lateral position the uppermost part of the beginning of the aorta will be the part without a coronary orifice, and therefore in this position the risk of coronary air embolism should be lessened It would be interesting to know on which side the patient was lying in cases of death from air embolism complicating artificial pneumothorax therapy

There are two reasons why in venous air embolism also the left lateral position is important (1) arterial (coronary) air embolism may complicate entry of air into a vein paradoxically because of a patent foramen ovale, (2) venous air embolism causes froth in the right ventricle but there is experimental evidence that this is less likely to block the outflow tract when the body is in the left lateral position[1]

No one doctor can speak from great experience of embolism, and when he meets this emergency and decided what to do it may be too late I think th artificial pneumothorax therapy, intravenous th and indeed in any procedure which might be compli by this or any other accident the doctor should, b starting, give thought to what might go wrong and w he would do if it did First-aid measures in air em should include turning the patient on to his left side *addition to withdrawing the needle (if any) and lowering* the head

Chase Farm Hospital,
Enfield, Middlesex C ALLAN BIRCH

FIBRO-ADENOSIS

SIR,—I have been expecting someone to comment your annotation of Jan 1 Under the heading of Fib adenosis it gave a brief summary of an investigat by Dr Kiaer on the potential dangers of (accordi to a footnote) fibro adenomatosis or chronic mastit The confused nomenclature makes it difficult to ass the value of any investigation

"Fibro adenosis" as a comprehensive title was sug gested by Atkins to include a number of structu changes in mammary tissue "Fibro adenomatosis," surely, is mostly a male affair, and covers the majori of enlargements of the male breast from childhood t old age The terms "chronic mastitis" and "chro cystic mastitis," inaccurate but harmless, originated fro the writings of Astley-Cooper (1828), Benjamin Brod (1840 and 1860), and Paul Reclus (1868) to become eve tually—in the opinion of Foote and Stewart—little mo than conditioned reflexes of the surgical mind.

At a later dater date Schimmelbusch (1892), Bloodgo (1923), and Cheatle and Cutler (1931)—who all, incide tally, combined the rôles of surgeon and histologist were mainly responsible for raising doubt on the inte pretation of one phase or histological pattern of "chro mastitis" still often referred to as Schimmelbusc disease This state of mammary tissue has been persisten regarded by histologists as pathological, depicting, effect, neoplasia of non functional tissue

For their impressions of a lump in the breast clinici are largely dependent on abnormalities of the grou substance, and, when histologists threw doubts i their minds about epitheliosis, microcystic hyperpla and other microscopic findings, something of a grievan was developed and gradually displaced on to lum breasts in general This misunderstanding bet clinicians and histologists—who often, so to speak, l far apart—brought "chronic mastitis" under suspi and was responsible for innumerable mastectomies, at any age, more especially during the 1920s and '30

The very nature of this subject, dating presumab from the emergence of the primates, does not permit clear cut clinical and histological divisions, nor for t matter of a satisfactory comprehensive title No unif standard of structure and function applies to ma tissue rather has it "a wide variation from time time and from individual to individual without in any other organ in the mammalian body" (Creigh Most of the common structural changes, however, roughly into two groups with a subdivision of second

1 Exaggerated physiological changes

2 Pathological changes Neoplasia { non-invasive / invasive and irreversible

In an important article[1] E K Dawson enters a that the terms "adenosis" and "fibrosing adenosis" hypertrophy of functional tissue during adolescence, adult life, with a pregnancy-lactation period, or regression from fertility—should be maintained escribe the first group Adenosis in this sense is neither disease nor a menace

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[1] T M, Long, J, Oppenheimer, M J *Amer Heart J* 269

[1] *Edinb med J* 1954, 61, 391

On the other hand, once a neoplasia is established, its estimation may be earmarked biologically, from the tart; yet histological confirmation one way or the other ay on occasion be near impossible A variety of physio gical and pathological patterns may be found in sections om different areas of the same breast These are often terpreted as stepping stones to disaster, but presum bly could be tissue reactions to a varying chemical tatus

London, W 1 — F D SANER.

PNEUMOCONIOSIS

SIR,—Dr Triger[1] has commented on the lack of com arisons of pneumoconiosis diagnoses during life with ost mortem findings, and Dr Fletcher[2] has subsequently rawn attention to the observer error in pathological sessment

This problem of comparing diagnoses intra vitam with st-mortem findings in silicosis has been repeatedly idied in Germany

> Worth and Nerroter[3] have analysed the data for 327 cases silicosis confirmed by necropsy The degree of silicosis was sed on the older classification into stages I II and III In 83% of the cases there was agreement between clinical d post-mortem findings for the degree of silicosis found king the necropsy findings as correct, the clinical results erestimated the disease in 8% of the cases and under timated it in another 8% The overestimates occurred iefly in stages 0–II and the underestimates in stage III.

Although the German classification is not appropriate r pneumoconiosis in coalminers and differs from the assification used in this country, a detailed survey ere would probably also show reasonable general agree ent between radiographic and pathological observations.

Safety in Mines Research Establishment
Ministry of Fuel and Power
Portobello Street
Sheffield 1
G NAGELSCHMIDT

RUPTURE OF DUODENAL STUMP AFTER GASTRECTOMY

SIR,—Mr Henson's paper (March 19) draws attention n afferent loop obstruction as a dangerous complication f a Polya partial gastrectomy The successful result his case emphasises the importance of his early and ccurate diagnosis of this complication which is gradually ecoming more widely recognised

With regard to his conclusions I would suggest that, n addition to careful clinical and radiological examina ions the gastric remnant should always be aspirated ith a Ryle's tube, when afferent loop obstruction is uspected Absence of bile in the aspirations will confirm hat the afferent loop is obstructed This simple test an be performed in a few minutes in the ward and may ive useful results particularly at times when the clinical igns are indefinite and radiological facilities are not mmediately available

Ilford Essex. — R P WARREN

SIR,—I was interested to read Mr Henson's article lthough I am not sure that a distended afferent loop er se will cause the blowing of a duodenal stump I feel hat it may contribute to this catastrophe With an nperfect duodenal suture line afferent-loop distension ould conceivably hasten the breakdown of the closure nd add to the violence of the burst

For four years I have been performing a Roux-en Y nastomosis in the Polya type of gastrectomy for odenal ulcer This operation results in deviation of e afferent loop from the gastro intestinal anastomosis d is undertaken to prevent the post gastrectomy syndrome We stated that a point incidental to the Roux en Y type of anastomosis was that the duodenal contents pass uninterrupted into the jejunum thus diminishing the risk of a blown duodenal stump[1]

My experience with the Roux-en Y anastomosis has been that, while a small number of minor duodenal leaks have been encountered (about the seventh day with little inconvenience to the patient), there have been no cases of catastrophic burst duodenal stump This may prove an important advantage My experience supports the claim that a distended afferent loop is an important factor in rupture of a duodenal stump

Victoria Hospital
Swindon Wiltshire
J EWART SCHOFIELD

PERFORATED DUODENAL ULCER AND SLEEPING POSITION

SIR,—Few will dispute that hyperchlorhydria is an important factor in duodenal ulceration The following investigation was suggested by the possibility that gastric and duodenal night secretions, collecting at the most dependent portion of that part of the gut, might there cause ulceration The most dependent portion will of course vary with the patient's position, but changes of position are very much less at night and so it seemed reasonable to expect some relationship between sleeping posture and the site of ulceration

One obvious objection is that the lie of the stomach is very variable for this reason gastric ulceration was ignored throughout the investigation. The position of the duodenum is also variable but the differences are comparatively slight. The anterior surface of the first part of the duodenum nearly always passes transversely from left to right with a slight tilt superiorly and posteriorly The digestive juices of the patient who sleeps on his belly will therefore bathe the anterior wall of his duodenum; and the juices of the patient who sleeps on his back will (though to a lesser extent because of the posterior tilt) bathe the posterior duodenal wall

This hypothesis may be criticised on the grounds that the gut is not a flaccid gutter that its walls are normally in apposition and that stagnant puddles of secretion are therefore unlikely to form. Yet at laparotomy the duodenum is usually found to be uncollapsed and peristalsis is less noticeable there than elsewhere in the small gut More difficult to counter is the suggestion that people do not know in what position they sleep—they know only the position in which they fall asleep During the night, if advertisements are to be believed vast amounts of energy are expended in twisting and turning Nevertheless careful observations on sleeping hospital patients reveal that major movements involving complete change of posture are made on the average some three or four times only and usually the patients revert quite soon to their favourite sleeping position Most patients become more restless towards morning but quite a number—particularly women—lie log like all night in one position

Sleeping posture varies considerably with age the young sleep more often on their bellies than do the old and more older people—perhaps because of fat bellies and less adaptable vertebral columns—sleep on their backs. Nevertheless, the most common position in all age groups is on the right side Slightly less common are those who sleep on their left sides Comparatively few persons sleep on their backs, and even fewer sleep on their bellies

100 patients who had had anteriorly perforated duodenal ulcers (confirmed at laparotomy) were first investigated. Those who had returned home were sent a questionnaire concerning their position during sleep, and the others were questioned verbally Many were unable to make dogmatic statements so the words always,' usually sometimes," and "never' were used in estimating the frequency of the four positions (right side left side back, or belly) When allowances had been made for intermediate positions, the findings were as follows:—

Chiefly on the right side	45%
Chiefly on the left side	33%
Chiefly on the belly	None
Chiefly on the back	22%

The average age of these patients was 48

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[1] Triger K. Lancet 1954 i, 74
[2] Fletcher, C. M. Ibid p 648.
[3] Worth G Nerroter W Beitr SilikForsch 1954 30 3

[1] Schofield J E. Anderson P St. G Brit med J 1953, ii 595.

137 outpatients and inpatients also of an average age of 45, but with no recognised abdominal troubles, were then similarly questioned, and the following results obtained

Chiefly on the right side	44 %
Chiefly on the left side	35 %
Chiefly on the belly	9 %
Chiefly on the back	12 %

Contrary to expectations, the results showed that patients who had suffered anterior perforations slept less often on their bellies than those in the control group There are two possible explanations for this the duodenal contents may be satisfactorily buffered, even in those with hyperchlorhydria, by the duodenum's own alkaline secretion and by the lessened nocturnal biliary and pancreatic contributions, a more probable explanation is that patients with anterior duodenal ulcers find that lying prone is more uncomfortable than lying supine 2 patients spontaneously admitted that, shortly before perforating, they had found that their pain was very much less if they turned on to their backs

My thanks are due to Mr Richard Charles and Mr Arthur Hill for permission to interrogate their patients

Ipswich EDWARD ELMHIRST

ARTIFICIAL POSITIVE-PRESSURE RESPIRATION

SIR,—When respiratory paralysis is associated with pharyngeal paralysis special precautions must be taken regarding artificial respiration Brown et al [1] emphasised the need for early tracheotomy, thereafter artificial respiration may be applied by means of a tank respirator [3] or by intermittent positive pressure (I P P) through a short cuffed endotracheal tube inserted directly into the trachea [3,4]

While some I P P machines are designed to intermit the flow from a cylinder of compressed air or mixture of oxygen and nitrogen,[5,6] many others are designed to pump room air rhythmically from a bellows [7,8], and with these a pressure operated (P O) inspiratory/expiratory valve must be used This type of valve is used in the positive pressure attachments with which many tank respirators are now being fitted [9] In prolonged I P P with a bellows type machine, the air passes through breathing tubes and a humidifier to the P O valve, then through a short piece of wide bore rubber tubing to a suction connection attached to the cuffed endotracheal tube The P O valve is of crucial importance, for it must respond promptly to the rhythmic alternation of inspiratory and expiratory pressures in the tubes, must seal accurately in either phase, must offer minimum airflow resistance (especially to expiration), must never stick, must be robust, and must be easily cleaned and sterilised

The P O valve described here was designed by one of us (G T S C)

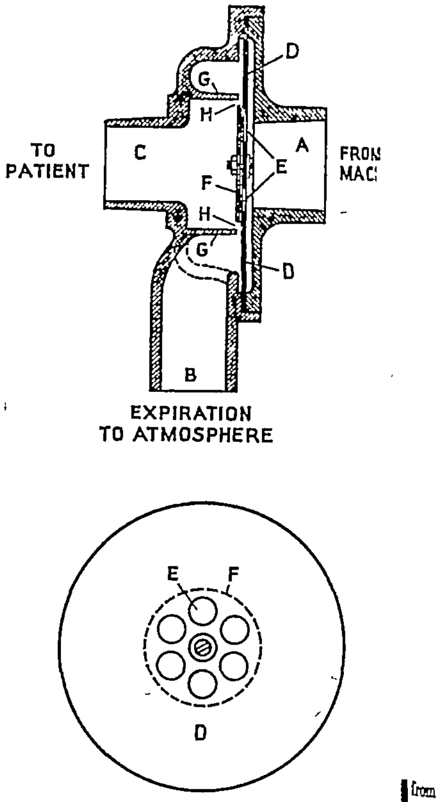

Fig 2—Above, diagram of the valve. Be diaphragm showing inspiration ports and p valves (interrupted line)

The valve (figs 1 and 2) consists of an aluminium casing with three ports—inspiratory (A), expiratory (B), and inspiratory/expiratory (C)—and a diaphrag (D) of reinforced rubber The casing is made in two par which are held together by hinged clips similar to those us on the distributor head of a car When assembled, the casi firmly grips the margin of the diaphragm The diaphrag has a ring of six air holes (E) and carries a thin central attached metal plate (F) and two studs which fit into corre ponding notches in the casing to ensure correct positionin With the diaphragm in neutral position a gap of 1/32 in sepa ates it from a circular sealing rim (G) which surrounds t inner aspect of the inspiratory/expiratory port By undo the clips and opening the casing the diaphragm may removed and a fresh one installed in a few seconds diaphragm and casing withstand sterilisation by boiling

On inspiration air is forced through the six air h simultaneously pushing the diaphragm against the rim and the metal plate away from the air holes expiration the diaphragm breaks away from the sealing and returns to its neutral position, impelled by suction the expanding bellows on one side and by pressure from recoiling lungs on the other and aided by its own elasticity The same forces seal the metal plate against air holes, compelling the expired air to pass through single expiratory vent (to which a spirometer may be atta when desired)

The combined area of the air holes and the area enc by the sealing rim determine the resistance of the valve airflow—which is up to 10 cm water pressure in inspi (varying with the condition of the diaphragm) and 2 water pressure in expiration The 1/2 in excursion (H) of diaphragm from the neutral position is crucial in val efficiency

The casing offers no lodgment for water condensing the expired air, provided the expiratory vent is downwards to allow drainage No sliding parts that stick or wear are used in the construction of the valve

Careful watching and frequent changing is necessary in use of any P O valve and a spare valve must always be hand The valve described here should be changed at daily, although it has been found to function effectively few days without attention, occasionally it may be suffic to change the diaphragm only The application of neg

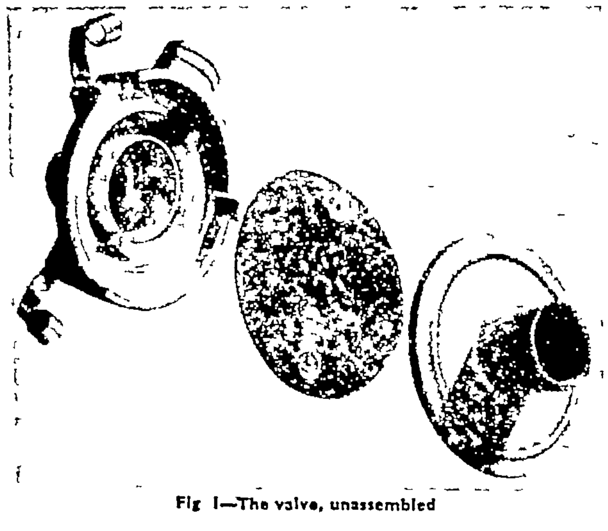

Fig 1—The valve, unassembled

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1 Brown, J R Baker, A B, McQuarrie, I J Amer med Ass 1947, 135 425
2 Harris H H Arch Otolaryng Chicago 1952, 56, 385
3 Lasson H C A Lancet 1953, i 37
4 Smith A C Spalding J M K, Russell, W R Ibid 1954, i 939
5 Bang, C Ibid 1953 i 723
6 Macrae J McKendrick G D W Claremont J M, Sefton E M, Walley, R V Ibid 1953 ii 971
7 Beaver R A Ibid 1953 i 977
8 Russell W R, Schuster E Ibid, 1953, ii, 707
9 Galpine, J F Ibid, 1954, i, 1013

ressure in expiration ("blow and suck") is advocated by aloney et al[18] but with a P.O. valve of this type suction ould interfere with closure in the expiratory position. In ny case, "blow and suck" action is not possible with the pparatus used at present in Britain. Future models will mploy mechanically operated valves rather than P.O. valves; he former will operate effectively in either I.P.P. or "blow nd suck" respiration, and will entirely remove the fear of alve failu[illegible]ould.

PPARATUS FOR TESTING POSITIVE PRESSURE EQUIPMENT

In assessing the efficiency of new apparatus it is ecessary to measure function against a standard. ccordingly one of us (G. T. S. C.) constructed a testing achine for I.P.P. equipment (fig. 3) in which a oncertina bellows acts as an artificial lung.

The relation (if any) of the expansile response of a patient's ung to the expansion of the bellows is not known, but the ellows works within the range of expected clinical pressures y expanding against a spring which, at a tidal volume of 20 ml., produces a pressure of 10 cm. of water. The expansion f the bellows is communicated through a simple lever system o a ball point pen moving to and fro along parallel guides. he mounting allows the pen to rest solely by gravity on graph aper, which is unrolled by clockwork at a constant speed. seconds recorder (also with ball point pen) works off an lectric-clock mechanism. A gauge indicates the pressure in centimetres of water) inside the bellows.

The inlet port of the machine will take a P.O. valve direct—orresponding to "mask" conditions—or will accommodate lastic tubes of two sizes, representing the male and female rachea respectively, into which cuffed endotracheal tubes an be inserted as in clinical practice in I.P.P.

The aim throughout has been to eliminate friction and erkiness, and so abolish adventitious movements of the ecording pen; the resultant curves are smooth and free rom unexplained fluctuations. They relate directly to ositive pressure and volume, but not to negative pressure, hough the latter shows on the curve and can also be read n the gauge. The device gives constant results under the ame conditions and thus can function as a reasonable standard. It has been indispensable in developing the P.O. valve described above and has been used to compare the performance of a number of such valves and of I.P.P. machines. The tester may also be used to measure the effect on airflow resistance of varying the other components of an I.P.P. assembly—e.g., the size of endotracheal tube.

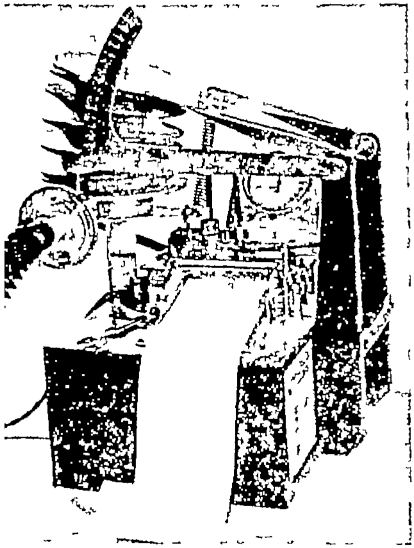

Fig. 3—Testing machine.

Coventry

J. F. GALPINE
G. T. SMITH CLARKE

Maloney J. V. jun., Elam J. O., Hanford S. W., Balla G. A., Eastwood, D. W., Brown E. S. *J. Amer. med. Ass.* 1953, 152, 212.

HYPERGLYCÆMIA AFTER BURNS

SIR,—It is some time since I discussed the occurrence of hyperglycæmia and glycosuria after burning injury with Dr. J. P. Bull and his colleagues at the M.R.C. Burns Unit in Birmingham. I was therefore very interested to read in Dr. Sevitt's letter (March 12) that he has found additional evidence of adrenocortical overactivity and also changes in the islets of Langerhans at post-mortem examination in such a case. Dr. Sevitt has misunderstood me in stating I suggested that early involvement of the islet cells did not take place. He is correct in presuming that the reducing substance in the urine of my patients was glucose, not lactose or galactose; *incidentally none of my patients were* treated with lactose powder. Finally, I described the effect of a single dimercaprol injection on glucose tolerance in the burned cases as slight. However, to my colleagues and me the implication of this, coupled with the more pronounced effects after several injections in some diabetics, is that replenishing or augmenting SH groups may alleviate faulty glucose metabolism in certain patients.

Medical Research Council
Clinical Research Unit,
Guy's Hospital, London, S.E.1

W. J. H. BUTTERFIELD

EFFECTIVE CIRCULATION OF UTERINE WALL IN LATE PREGNANCY

SIR,—Dr. Schuurmans (March 26) in accounting for the efficiency of anti-histamine treatment in pregnancy toxæmia has advanced hypotheses which much evidence refutes.

He assumes that permeability of the maternal capillaries exists in pre-eclampsia to account for the œdema. This cannot be the case, for the protein in œdema fluid amounts to 0·10–0·48 g. per 100 ml.—a level insufficient to overcome the osmotic pressure and attract fluid out of the vessel wall.[1–4]

Nor can adrenaline or noradrenaline be invoked in the causation of hypertension, for it has been shown by Assali[5] that benzodioxane effective in producing adrenergic blockade was without effect on the blood-pressure in normal or toxæmic pregnancy. Corticoids, too, cannot be of primary ætiological significance,[6] since their function appears to be regulatory. Further, the level of the lipid-soluble substance in the urine, a reflection of the corticoid content of the blood, does not correspond with the severity of the toxæmic state,[7] and therefore is not consonant with the ætiological importance of corticoids—*a fact confirmed by the failure to provoke* toxæmia in pregnancies other than the first. Contrary also to Dr. Schuurmans's contention, evidence has accumulated in recent years to show that histaminase activity is unchanged[8] or is even considerably reduced in pre-eclamptic toxæmia.[9,10]

*There would, however, appear to be another explana*tion for the therapeutic effect of anti-histamines, based on their effect in overcoming renal spasm. Chatterjee[11] has administered these substances in resistant cases of

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1. Dexter, L., Weiss, S. *Pre-eclamptic and Eclamptic Toxæmia of Pregnancy.* Boston, 1911.
2. Stead, E. A. jun., Warren, J. V. *J. clin. Invest.* 1944, 23, 283.
3. Switzer, J. K., et al. *Amer. J. Obstet. Gynec.* 1950, 60, 427.
4. Helmuth, K., Albano, J. Cited by Switzer et al. (footnote 3).
5. Assali, N. S., Pyrtakowsky, H. *Surg. Gynec. Obstet.* 1950, 90, 655.
6. Sophian, J. *J. Obst. Gynæc., Brit. Emp.* 1955, 62, 4.
7. Venning, E. H., Singer, B., Simpson, G. A. *Amer. J. Obstet. Gynec.* 1954, 67, 542.
8. Gabwray, B., Anrep, G. V., Barsoum, G. S. *Int. physiol. Cong., Copenhagen* 1950, p. 212.
9. Kapeller-Adler, R. *Ibid*, p. [illegible]50.
10. Kapeller-Adler, R. Ciba Foundation Symposium on Toxæmia. London, 1910.
11. Chatterjee, H. N. *Lancet*, 1952, ii, 90.

anuria, the sequel of severe cholera, with remarkable success Here the only possible explanation for their effectiveness was that they overcame the basic renal ischæmia responsible for the renal failure It would be reasonable to conclude that Dr Schuurmans's success is similarly explained; for I have shown[6] that such a renal state, provoked by the resistance to stretch of the myometrium, underlies the toxæmic process

London W 1 JOHN SOPHIAN

THE PSYCHIATRIC DAY-HOSPITAL

SIR,—In your annotation of Feb 26 the reference to the paper from Bristol on this subject should read, not Aron, K W, but Aron, K W, and Smith, S The Bristol day hospital experiment was initiated, and is still being conducted, under the general supervision of Dr Smith

Ayr K W ARON

INFECTION WITH CRYPTOCOCCUS NEOFORMANS

SIR,—In the absence from this country of Dr Beck, and as the one associated with him in case 1 of our article (March 12), may I reply to Dr Michaels (March 19)?

I think that he is interpreting too rigidly the phrase "revealed the true nature of the illness" He will no doubt have noticed that in our discussion we referred to the *association* between cryptococcosis and Hodgkin like lesions, and that we had also considered that in these cases the explanation might lie in an alteration of certain immunity mechanisms However, the statistics of the series we cited suggested that the explanation may not be quite so simple as that and it was this thought we had in mind.

I have had the opportunity of seeing a section of a lymphatic gland which showed cryptococci in typical Hodgkin tissue, this gland had been removed in the early stages of generalised lymphadenopathy

In our case 1 the cryptococci were present in large numbers in the sample of cerebrospinal fluid taken on admission before any antibiotics had been given. I believe, too, that Dr Michaels will find that a large proportion of the cases in the series reviewed by the authors we mentioned occurred before the days of antibiotics

Morbid Anatomy Laboratory,
St Margaret's Hospital,
Epping, Essex
I M TUCK

B C G VACCINATION

SIR,—Dr Webster (March 5) asks very pertinent questions regarding this prophylactic measure and quotes Prof Heaf (Feb 12) "statistical proof is difficult to obtain" May I give my views on some of these points in the light of tuberculin-sensitivity surveys of the school children in Lewis in 1949 and 1954 and the administration of B C G vaccine

I was extremely keen on pressing on with administering B C G to every tuberculin negative person—young or old—whom I could discover, because of the exceptionally high mortality rate (1948, 176 per 100,000, 1954, 76) and the sustained high notification rate with 50% of all notified cases yielding positive sputum, and the abnormally high infection rate among school entrants (5–6 years) of 18% A high positive reactor rate in this group must surely imply many infectious cases in the population, and a falling off of this rate likewise must indicate a diminution of these Such a fall was observed on a second tuberculin sensitivity survey in 1954, when the rate was down to 2 7% for entrants In view of this I concluded that there did not seem the same need to push B C G The death rate fell to about 12 per 100,000 in 1954

This glorious result could not be attributed to B C G—it was a natural fall consequent on improved social conditions and better treatment of infectious cases However, closer study of the figures (March 19, p 620) suggested that the higher the positive reactor rate in any area the lower the mortality, seeming to indicate that immunity is related to allergy Again allergy as produced by B C G appears to give enh[illegible] resistance By September, 1954, of 3000 vaccinated (the majority three or four years previously) none had [illegible] notified as tuberculous whereas of 1188 positive reactors 1949 29 had been notified, and of 2814 negatives 9 had [illegible] likewise notified, and since September, 1954, several positive and negative reactors have been [illegible] requiring sanatorium treatment In view of [illegible] once again instituted a vigorous B C G campa[illegible]

With regard to unpleasant consequenc[illegible] have only 3 cases of axillary adenitis with absce[illegible] because the long time necessary for healing of the [illegible] have gone in for vaccination by multiple pu[illegible]cture after concentrating the vaccine as supplied, by [illegible]ntrifuging and discarding 50–80% of the supernatant liquid (I a[illegible] endeavouring to find the most suitable concentration) The subsequent local reaction, which appears in fro[illegible] seven days onwards, is slight, has had no undesirab[illegible] side effects, there is no ulceration or scarring, and th[illegible] skin over the vaccination area simply desquamates I[illegible] 50 cases so vaccinated the "take" has been 100%, an[illegible] the conversion rate has been 100% also The conversio[illegible] time is much shorter than by intradermal injection Th[illegible] perfection of this technique would mean enormou[illegible] advantages and would allow mass B C G vaccination t[illegible] be undertaken with ease by school medical officers an[illegible] general practitioners With Heaf multiple punctu[illegible] apparatus a single test only is necessary Where loca[illegible] authorities provide segregation homes the short[illegible] conversion time would mean a considerable saving Fo[illegible] this multiple puncture technique I would suggest that [illegible] suitably concentrated vaccine should be put up in sing[illegible] doses in capillary tubes as is done with calf-lymph

Dr Loxton (March 19) mentions desensitisation b[illegible] artificial means I have scores of children reverting t[illegible] negative (to 100 T U) naturally, and over a score wh[illegible] showed radiological evidence of infection and yet hav[illegible] lost their hypersensitivity to 100 T U When B C G w[illegible] administered to some of these they once again becam[illegible] positive Again, some B C G reverters after three yea[illegible] were revaccinated by multiple puncture, and the loc[illegible] and allergic reaction appeared simultaneously in less th[illegible] seven days How does this fit in with Godlowski'[illegible] enzymatic hypothesis?

I am convinced that B C G confers immunity of a hig[illegible] degree No special precautions regarding segregatio[illegible] were taken here, and the majority of vaccinated childre[illegible] live in the areas with the high sputum-positive rat[illegible] should like to see all babies given B C G at birth

Stornoway, Lewis R STEVENSON DOIG

THE ACTION OF CHLORPROMAZINE

SIR,—I have read Dr Buxton Hopkin's accou[illegible] (March 19) of the French work dealing with the so calle[illegible] "phenomena of Reilly" with bewilderment

> These effects, we are told, follow "irritation as oppo[illegible] to either simple section or stimulation of sympathetic nerves"[illegible] they are produced by "perisplanchnic injections of differe[illegible] substances," and, "physical agents—e g, trauma an[illegible] electrical stimulation." The condition is rapidly fatal and [illegible] accompanied by widespread lesions, including hæmorrha[illegible] and necrosis of the suprarenal glands as a constant featur[illegible] The "irritation" of the splanchnic nerves produces co[illegible]spicuous changes in the cerebral circulation. "Pathogen[illegible] impulses" pass from the brain to the periphery "Th[illegible] effects are produced by placing irritants in direct cont[illegible] with or in close proximity to autonomic nerves in amou[illegible] which would be innocuous by injection elsewhere"

The results described are so strange and unexpecte[illegible] and the explanations offered are so much at varian[illegible] with current physiological thought that I for one pref[illegible] to suspend judgment until this experimental work ha[illegible] been repeated and confirmed by reputable worke[illegible] elsewhere

Department of Physiology,
Middlesex Hospital Medical School,
London W 1
SAMSON WRIGHT

MASKED EPILEPSY

SIR,—Some children have periodic attacks of headache, or abdominal pain, or vomiting or limb pains or fever, and these five symptoms may be grouped together as the recurrent syndrome Dr Wallis (Jan 8) suggests that many perhaps all of these children may have epilepsy I agree with Professor Illingworth (March 26) that it would indeed be a tragedy if all of this large group of children were deemed to be epileptics, and I doubt very much whether it is true From clinical experience I am satisfied that each of the five symptoms can be the bodily *manifestation of a tension state* and the common factor to them all is tension Recurrent abdominal pain in children, for example, fulfils the criteria of a stress disorder,[1] and it usually clears up after measures have been applied to relieve the tension Giving phenobarbitone, which Dr Wallis recommends, is one such measure, but this is a palliative treatment only Thorough treatment involves exploration of the child's mental state and his home environment, this takes time but the time is well spent because after treatment the child and his mother are better adapted to their lives and more content

London W 1 DESMOND O'NEILL.

SIR,—When a new idea appears one can either disbelieve it or try it out I have heard of a famous surgeon who was wont to raise a laugh in the operating theatre by saying "Close the door sister; we don't want one of Mr Lister's germs to creep in" The laugh is now (to mix metaphors) on the other foot

Professor Illingworth prefers disbelief to experiment, but the letter, in the same issue from Dr Ulutin, shows that experiment is more rewarding I will not attempt to answer all the points raised by Professor Illingworth Most of them have been dealt with in my paper

For instance he says that attacks of fever are not manifestations of epilepsy whereas in my description of case 2 I showed that the child was in hospital suffering from an unrelated disease and the attacks of fever and vomiting were observed by competent clinicians but could not be explained He has also neglected the experience of Davidson and Lombroso which I cited.

I should, however like to comment on three-month colic.

Professor Illingworth says I can see not the slightest connection or resemblance between three-month colic and epilepsy After reading his exhaustive paper on the subject[2] one is driven to the conclusion that no-one knows the cause of this malady But there are several clues to its nature: first the experience of Sir Frederic Still and Dr W Sheldon, cited by Professor Illingworth, that in some cases the condition leads on to convulsions; second the comment[3] that the disease is apt to run in families and may be linked with a particular kind of temperament; third the experience of Dr Millichap who states (Feb 19) that some of his patients with cyclical vomiting had had colic in infancy

I can think of four ways in which this hypothesis might be tested first to inquire into the family history of those children who suffer from three-month colic; second to take electro-encephalograms from them; third, to try the effect of *anticonvulsant drugs* and *fourth, to follow them into later life* and see if they do develop convulsions. The first three methods have not been tried as far as I know Until Professor Illingworth has used them I must consider his dogmatism unjustified The fourth seems promising in view of the work of Still, Sheldon and Millichap

As to the mode of onset I know that Sir William Gowers liked to hear of a sudden onset before making a diagnosis of epilepsy But, as someone has written he spoke without benefit of electro-encephalography No doubt he would now be the first to admit that the sort of cases he described in *The Borderland of Epilepsy* should really be included within the limits of that disorder

Some may think that we are arguing about something that does not matter—i.e., a name. I feel very strongly that it is important that these conditions should be recognised and *treated*. Children still die from cyclical vomiting[4] Now that the nature of the condition is known there is no excuse for this to happen

Professor Illingworth complains that hospitals will be inundated with requests to investigate obscure pains, vomiting and fevers. Surely the more such cases that are investigated the better

Bath. HUGH R E WALLIS.

STERILISATION OF SYRINGES

SIR,—About five years ago I gave up wrapping syringes in lint or gauze before boiling them, for I found I could do so without the glass breaking It may be that the holes in the tray of my steriliser are of the right size (they are about $^1/_4$ in. in diameter), but I believe this is a very usual size in sterilisers My original reason for abandoning lint was because I disliked unwrapping syringes with a hot wet compress round them—particularly when in a hurry At the present price of lint and gauze their omission saves money as well as time

Manchester 16. S SHUBSACHS

PERIODICALS FOR OVERSEAS

Mr Mark Gibbs, senior history master at the Grammar School Audenshaw Lancashire writes: "Very many students in overseas schools and colleges would welcome second hand copies of THE LANCET and similar journals, which they are unable to afford for themselves. The senior boys of this school (already operating a periodicals scheme for refugees) are therefore starting a posting scheme to be known as Periodicals for Overseas. We already have the addresses of some 40 colleges which have asked for supplies, and we can provide helpers with ready addressed labels and ample instructions for posting Further details will gladly be sent on request. Journals should *not* be sent to Audenshaw

Parliament

Genetic Effects of Nuclear Explosions

ON March 22 Dr EDITH SUMMERSKILL asked the House of Commons to consider the long term and remote effects of continuing nuclear explosions and the dangers of continuing radioactive contamination of the world's atmosphere particularly to future generations. Scientific investigations in this field must necessarily be limited, but we would she held be *irresponsible to ignore the* reports that had been made. To date there had been 65 nuclear explosions—50 by the Americans, 12 by the Russians and 3 by the British—and scientists were now expressing the opinion that these explosions could not continue without the danger of serious damage to health

The professor of biophysics in the medical school of Osaka University in Japan, had reported in people exposed to the Bikini test explosion of March, 1954, serious injury to the blood forming organs and the reproductive organs Undisputed evidence showed that a pregnant woman, exposed to only a moderate dose of radiation, ran the risk of aborting or giving birth to a stillborn child

The Federation of American Scientists, she continued, had suggested that the United Nations should appoint a commission to explore the dangers of continued nuclear explosions Mr Strauss the chairman of the Atomic Energy *Commission of the United States*, had reported that the fall-out from the hydrogen bomb could contaminate an area of 7000 square miles with lethally radioactive material. In this country Lord Adrian had said that the hydrogen bomb might "lead to a degree of radioactivity which no-one can tolerate or escape and thus end the human race"

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[1] Mac Keith R O'Neill D *Lancet* 1951 ii 278
[2] *Arch. Dis Childh.* 1954 29 165
[3] Annotation *Brit. med J* Jan 8 1955 p 93

[4] Brown R J K *Ibid* 1951, ii 1033

Mr IAIN MACLEOD, who stressed that he spoke on behalf of the Government, agreed that this problem offered a personal challenge to everyone which could not be shuffled off on to our leaders, on to our leader-writers, or on to the scientists Turning to steps already taken, he said that the Medical Research Council had had committees considering the subject for eight or ten years Represented on these committees, which were not Government bodies, were leading authorities from the universities, from the M R C research staff, and from the atomic energy authorities

There was nothing new in human beings being exposed to radioactivity We, and our ancestors, and all our evolutionary predecessors, he pointed out, had been exposed to radioactivity from outer space Each of us absorbed natural radiation of about 0 1 rontgen each year According to the U S Atomic Energy Commission the total amount of radiation received by residents in the United States from all nuclear detonations was about 0 1 röntgen Our calculations, derived from the Atomic Energy Authority, showed that the figure for somebody in this country would be about 0 03 rontgen This figure was based on the improbable assumption that a man stands outside in the open for 24 hours a day for about 50 years The effective average dose would in fact be considerably less Indeed, at the present levels of irradiation it seemed improbable that we had anything more than an interesting basic scientific problem and a situation which must be watched very carefully indeed

The real question, of course, was what was the threshold of radioactivity (which, if we are not there yet, we may reach in the future) beyond which man's genetic constitution might stand at risk The dose of radiation accepted as a maximum level for workers on radio-isotopes or for radiologists was 0 3 röntgen per week, or, taking working hours and holidays into account, about 15 röntgen a year That was enormously greater, of course, than any of the figures which the House had been discussing, but where large numbers of the community had to be considered the number of genes at risk was enormously increased, and therefore the number of matings which might be harmful was also increased He had tried to find a figure at which danger would begin, but the more he went into the subject the more he found that the scientists disagreed Estimates of the dose of radiation over a generation that was likely to double the spontaneous mutation-rate had varied from 3 röntgen to 300 rontgen He was told that 50 rontgen over 25 years was as good a guess as could be made The increase in the United States of America had only been a tiny fraction of this, and in this country it had been still smaller

The United States Atomic Casualty Commission had been studying the population in the vicinity of atomic explosions during the late war There was evidence that some conditions had a higher incidence among these populations, but no statistically significant evidence of genetic damage Studies of people such as radiologists and patients who for therapeutic reasons had to have considerable doses of radiation had not shown any evidence of genetic damage Dr BARNETT STROSS interposed that an American study of women treated with radiation for menorrhagia showed that among them the incidence of children born with congenital heart-disease and dislocation of the hip and clubfoot had increased

In this country, Mr MACLEOD continued, research was proceeding under the auspices of the M R C in the research unit at Harwell, and there were other research institutions at Hammersmith Hospital and Leeds The work was also being supported in many university departments For the M R C's work in their own establishments on all aspects of the effects of radiation £208,000 was allocated in the provisional estimates for 1955–56 If the council found that an increase was essential, this would have the favourable consideration hancellor of the Exchequer

The Problem of the Aged

In the House of Lords on March 28, Lord BEVERI suggested that many of the social and human problem of the aged were due to the fact that though the dec of our faculties was inevitable, the rate at which it car was uncertain The change in the age-structure of population also created difficulties In 1951 we ha 6,750,000 people of pensionable age, and about the sam number of working age, and fewer than 6 million children By 1979 there would be 9,500,000 people of pensionable age and there would still be about the same number of people of working age The Chancellor of the Exchequer would have to find something like £500 million a yea for pensions over and above what was paid by national insurance

But the problem, he maintained, was not mainly one of money The economic and social problems of the aged could not be solved by simply handing money to the pensioners Besides pensions old people needed care of many and different kinds—care of a perpetually changing amount and character, ranging from the car needed by those chronically sick in hospital, through occasional medical and nursing treatment, to perhaps no care at all The natural agent for giving care to old people was the family, but owing to the change in the population structure the family today was not physically able to do as much as formerly

The aim should be to keep the elderly in their own homes, but if this was to be done there should be adequate machinery for discovering the growing failure of strength which made transfer to a hospital, or other treatment necessary to avoid human tragedy The National Assistance Board did its work well, but it had only 1,250,000 old people on its books and there were 7 million elderly people In each neighbourhood there should be someone to whom neighbours could report an old person in need of more care At present something like 1 million elderly people were living by themselves, and old peopl trying to live in their own homes should have adequat help The present provision of home helps—30,000, o whom 3000 were full-time and 26,000 part-time worke —was ludicrously small

There must also be some half-way houses between t hospital providing full treatment and the home Loc authorities were empowered under the National Heal Service Act to establish these homes, and the powe had been largely used A number of local authoriti had also lately asked the Ministry of Health for pe mission to provide a chiropody service as part of t N H S, but the Government had replied that they h other, and greater, priorities for the health service Lord Beveridge's view the £14 million subsidy to cheape tobacco for all pensioners, many of whom were wome could be more usefully spent on providing home hel and chiropody

Lord AMULREE, returning to the problem of findin out in time when an old person is in need of care an help, said that the London borough where he worke had a population of 140,000 During the last six month roughly 200 old-age pensioners of sixty-to sixty fiv had applied for admission to hospital 90 of them live alone, and of these 40 were living in a state of dirt an squalor Most of them were so neglected that the needed a lot of good food and tidying and cleaning u The tragic thing was that in six months in one Londo borough 40 people were living in such conditions Wh an enormous reservoir of human misery must exist the rest of the country

The EARL OF SELKIRK, replying to the debate, said th old people should be enabled to remain at work as l as possible, to remain in their own homes, and never to fe that they had ceased to be part of the communit The home-nursing service was still expanding, th number of nurses employed had risen from 7700 in 19 to 9500 in 1953, and the number of cases attended h increased by about 40% He agreed that the number home helps was only 30,000, but in 1948 it had b only 11,000 There were also sitters-in and n watchers provided by some local authorities a voluntary organisations The money spent on tobac was an example of the unsatisfactory result of making benefits available by coupon, but in practice it was difficult to withdraw concessions, Chiropody was available in hospitals and in some clinics, and home treatment could be provided under the National Assistance Act, but he agreed that the service was inadequate An automatic method of discovering people who were in hardship was difficult to visualise Surely this was a matter in which anyone, whether it be a neighbour a general practitioner, or even a rent collector, could act by *reporting the circumstances either to the local council or to* the National Assistance Board He thought that more was being done in the way of coördination of services than was generally appreciated He believed that it was hoped shortly to institute meetings between medical officers of health *and general practitioners* *Local authorities* in ngland and Wales had provided 60 000 beds, of which at ast 50 000 were available for aged persons. Since the id of the war some 800 new small homes with accom odation for 23,000 people had been opened by local thorities. There were registered over 1200 small omes with another 23,000 beds He felt that whatever ction we took it was essential that old people should main useful, *independent*, and wanted this objective epended as much on each citizen as on the State

QUESTION TIME

Tuberculous Patients in Swiss Sanatoria

Replying to a question Mr MACLEOD said that the Ministry f Health began to send patients *to Davos in the autumn of* 951 when waiting lists for tuberculosis beds in England nd Wales stood at over 7000 The provisional figure for he end of 1954 was 2500 and this of course included a large umber of patients who were on the point of being admitted t once. Several hospital regions now had virtually no waiting st. Some were closing tuberculosis beds or turning them over o other purposes. Well over 900 patients from England and Vales had been sent to Switzerland by the National Health ervice, and this had been a most valuable contribution to he work against respiratory tuberculosis. But taking into ccount the diminished pressure today on tuberculosis beds t home and the recent difficulty in finding enough suitable atients willing to go to Switzerland for treatment he was atisfied that there was no necessity to extend the scheme eyond this autumn, when the contracts with the sanatoria xpired Suitable arrangements would be made for winding t up so as not to discharge patients from the sanatoria in Davos before they were fit

Commander T D GALBRAITH in a statement on the Scottish scheme said that over 900 patients from Scotland had gone to Switzerland During the past twelve months the total waiting list had fallen from just under 2000 to around 500 Chest physicians *were finding it increasingly difficult to* fill the beds in Switzerland. Patients were now coming forward from four areas only—Glasgow Renfrewshire Dunbartonshire and Stirlingshire They could not usefully send any more patients to the Sanatorium Wolfgang where they had had the use of 70 beds. For the present they were continuing to send patients to the Sanatorium du Mont Blanc where they had the use of 120 beds, which would be sufficient to accommodate all the *patients* coming forward under the scheme If present trends continued the *time might not be far distant* when it would be possible without prejudice to the treatment of Scottish patients to reduce still further the scale of these arrangements and eventually to terminate them altogether

Counteraction of Nuclear Explosion Effects

Replying to a question Mr HAROLD MACMILLAN, Minister of Defence said that experiments had been started under the *authority of the Minister of Supply to test the uses of smoke* in counteracting the effects of nuclear and thermonuclear explosions. The results would be of interest both to Civil Defence and to the Services.

Conservative Dental Work in Scotland

Replying to a question Commander GALBRAITH said that the number of courses of dental treatment other than emergency extractions and the supply of dentures, *in Scotland* increased from 603 000 in 1951 to 715 000 in 1954 Most of these courses were for conservative work

Obituary

HENRY MARRIAN JOSEPH PERRY

C.B., O.B E., F R.C.P L.R.C.P I

Major-General Marrian Perry director of pathology at the War Office in the early part of the late war, died on March 23, at his home at Walton-on Thames, at the age of 71

Son of the late John Perry he was educated *at Queen s* College Cork, and joined the Royal Army Medical Corps soon after qualifying in 1906 In the 1914–18 war he was a regimental medical officer, commanded a field ambulance, and became assistant adviser in pathology in France In 1918 his experience of agglutination tests *for* enteric infection in men inoculated with T.A.B vaccine was described in a long paper in our columns, with a note by Sir William *Leishman* Meanwhile he had investigated with Captain (now Sir Henry) Tidy an epidemic of aertrycke infection at a depot, and their account of this was one of the early special reports of the Medical Research Committee His bacteriological work continued with *contributions on bacillary dysentery, on the* anti genic properties of ' Bacillus psittacosis, ' on leishmaniasis, and on the flocculation test in syphilis. Some of it was done as assistant professor, and later professor, of pathology at the Royal Army Medical College but in 1926 *he was seconded from* Millbank to work for four years as director of the public health laboratories in Cairo To this period belongs the essay on the practical diagnosis of typhoid and paratyphoid infections which he and H J Bensted wrote for the Medical Research Council s *System of Bacteriology* (1929)

Returning to pathology at Millbank, Perry was appointed honorary surgeon to the King in 1933, and reached the rank of *major* general in 1935 As Director of Pathology at the War Office he was chairman of the Army Pathology Advisory Committee *and also a member* of the Chemical Defence Committee From these posts he retired in 1941

Marrian Perry will always be remembered as a brilliant teacher by all officers who attended his lectures at the Royal Army Medical College, writes L T P

One of his many gifts was his extraordinary command of English which always fascinated his students and at times delighted them by the artistic way he would round off his sentences His enthusiasm for his subject, and the energy he displayed, never failed to inspire He was quick, dapper and courteous, and as he entered the lecture theatre—always immaculately dressed—his commanding presence immediately *arrested attention.* He would take great care to make his subject interesting and to relate it to other branches of medicine An hour s lecture would slip away into what seemed like moments He had the gift of displaying facts in a simple way—always the mark of a good teacher

In his capacity as *Director of Pathology* he was exemplary in the high standard he set He lived for his subject and for the health of the *Army and would* go to endless trouble to further research. The team spirit in his department was indeed high, for he inspired confidence and was sympathetic and approachable Those who specialised in *pathology under* his guidance have cause to be grateful for the help and encouragement he gave them Among his colleagues in all branches of *medicine* he was held in high esteem and his opinion was sought on many problems. His judgment was sound; this had the effect not only of enhancing his own *reputation but also that* of his department In the mess he was the best of company and with his quick repartee a most entertaining after-dinner *speaker* *His many accomplishments* and his wisdom made him a unique personality in the Corps. The name of Perry will always be linked with the highest *traditions* of pathology in the Army "

General Perry was appointed O.B.E. in 1919 and C.B. in 1937, *and in 1941 he was elected* F.R.C.P He married in 1912 a daughter of the late E G Brower

AGNES CATHARINE SCOTT

C.B E., M.B Lond

Dr Agnes Scott, who died *in* London on March 22 had given many years of life and valuable service to India as chief medical officer of the Women s Medical Service

She was born in 1875, the second daughter of Canon John Scott of Leeds, and went to school at the Leeds Girls' High School and Yorkshire College She studied medicine at the London School of Medicine for Women and qualified in 1901 She had entered the medical profession with the definite idea of serving as a missionary in India, and she went out to that country in 1903 to serve with the Cambridge Mission to Delhi Her first years were spent in Karnal, a small station in the South Punjab, and afterwards she was moved to Delhi Both experiences were valuable to her in her later work since one was a rural area and the other an urban one The hospital in Delhi was at first in the middle of the old city, but during Dr Scott's time it was moved to the " Civil Lines " where there was more air and space. The experience of helping to build a new hospital was also valuable for her subsequent work

In 1917 a partial breakdown in health led her to accept the post of assistant to the inspector-general of civil hospitals in the Punjab This post had been created only a few years before and was first held by Dr M I Balfour, whom in 1924 Dr Scott again succeeded as chief medical officer of the Women's Medical Service In 1925 she was awarded the Kaiser-i-Hind gold medal and in 1932 when she retired she was appointed C B E

R Y writes " Dr Scott's gifts were essentially practical In the Punjab she was interested in the building and equipment of small hospitals in rural areas as well as encouraging existing mission and government hospitals in larger centres She also did much to improve the practice of midwifery in rural areas by encouraging the training of the Indian midwives and the creation of assistant nurse midwives who were capable of simple nursing and midwifery

" She showed the same gifts when she became head of the Women's Medical Service It was a time of change and development in India, and medical women shared in both Dr Scott realised that the service would ultimately be an Indian one and she was anxious that those who entered it should be well qualified for their responsibilities She also grasped the need for specialisation among some members of the service, particularly those who might become members of the teaching staff of the Lady Hardinge Medical College For this purpose she created the ' training reserve ' of the service by which promising graduates of Indian medical colleges could be sent abroad on scholarships She was interested in all forms of health work and she fostered their development Her devotion to high standards in professional work and her personal integrity were an outstanding example to members of the service

" Dr Scott was a keen churchwoman, and after her retirement she gave much time to the work of medical missions Her wide experience made this a valuable piece of service By nature she was reserved and not easy to know, but her occasional hot temper was a human touch which was accompanied by a sense of humour and a love of dogs Behind her reserve was a warm heart which showed itself in many kind thoughts and actions and in real devotion to her friends and to the Church "

FREDERICK HECTOR SCOTSON

M.B Manc and Lond , F R C.S

Mr Scotson, consulting surgeon to the Crumpsall Hospital, and Northern Hospital, Manchester, died on March 23 at the age of 55

He was born in Manchester, where his father was a well-known general practitioner, and he was educated at the Grammar School and the university where he won prizes and distinctions He continued his medical training at St Bartholomew's Hospital, and in 1922 took his London and Manchester degrees, the latter with honours He took his F R.C.S at the age of 24, but he had to wait a year for his diploma on account of his youth He held the usual resident posts at the Manchester Royal Infirmary, where he was a notably successful resident surgical officer

He visited the Mayo and other American surgical clinics before he started consultant practice in 1929 He on appointed to the staffs of the Crumpsall, t' ster Northern, and the Manchester Victoria Memorial Jewish Hospitals, and he helped to establish St Joseph's Hospital, a big Catholic charitable nursing home He was also a lecturer in surgery at the university As a general surgeon he had a busy life, but he found time for specialised interests His early writings on genito-urinary surgery included papers on malignant tumours of the kidney and testicle More recently he had turned to the surgery of the gastro-intestinal tract, and he was due to give an account of his experience in the treatment of peptic ulcer as his presidential address to the section of surgery of the Manchester Medical Society

W B , writing of Scotson's early days, recalls how " during his term as R S O he succeeded in breaking the rule against marriage, a cleverly handled and notable triumph. Later in the few respites he could snatch from his work he loved a holiday where he could ski or bathe in sunshine He was a good swimmer, having won his colours at the university, and continued to take active interest in the university swimming club He was a keen golfer and tennis player There can be little doubt that the energy he put into his surgical work brought on the illness which had troubled him in the last nine months "

Mr Scotson leaves a widow and four children, the eldest of whom is a medical student

RONALD GREAVES LADKIN

M.B E , M.A , B.M Oxfd, D.P.H

Dr R G Ladkin, senior medical officer in charge of health education in the Uganda medical department, died at Kampala on March 14, at the age of 35, from poliomyelitis

Educated at Kingsbridge Grammar School and Exeter College, where he was Stapledon scholar and Devon scholar, he graduated in medicine at Oxford in 1942, and was house-physician at the Radcliffe Infirmary He joined the Uganda medical department as a medical officer in 1943, and after serving in several districts became lecturer in anatomy at the medical school of Makerere College, Kampala At Mulago Hospital he undertook genito-urinary surgery and thus became interested in venereal diseases Of these he made a special study, and after taking his D P H. in 1948 he visited Trinidad to see methods of prevention and treatment in that area On his return to Uganda he became medical officer of the rapidly advancing Mengo district and was soon promoted to be in charge of the province of Buganda

It was in these country districts that he showed exceptional talent and industry, throwing himself with great energy and understanding into many measures of public health He developed quite new approaches to the problem of rural health in tropical Africa health weeks and large demonstrations along novel lines were held at many centres His achievements in this field won him appointment as M.B.E , and a new post was created for him at medical headquarters, Entebbe Both within and outside the territory he was in much demand, for he had a knack of combining the latest methods of visual education with a close knowledge of the African countryside and the psychology of the peasant farmers He had built up a unique collection of films, posters, and booklets, and he received grants from international organisations to promote the work of health education

A colleague writes of his " endearing personality which attracted his associates and won a place of real affection among the many Africans whom he served so generously He saw more clearly than most the factors responsible for disease and malnutrition in Africa He was essentially creative in all his work, full of good spirits, counting nothing of the financial stringency and other exacting conditions under which he worked He seemed to take a special delight in long spells as a fast bowler under the tropical sun and in himself carrying parts of the huts that were assembled to accommodate climbers on the upper slopes of Mount Ruwenzori He revelled in difficulties, not only those considered spectacular but those which were more prosaic For instance, the su of the Red Cross blood-transfusion service in owes a great deal to his skilful propaganda in spite much superstition among those Africans whom he endeavouring to help He felt that health edu which consists in changing the minds of people, would always be a difficult affair '

Dr Ladkin married Miss Heloise Carter, a nursing sister of the Uganda medical department, and there are three children

Medicine and the Law

Air Embolism during Artificial Pneumoperitoneum

At an inquest on a woman of 23 who died during the course of an artificial pneumoperitoneum injection for pulmonary tuberculosis, the cause of death was stated to be air embolism from accidental injection of the air into a vein. The operation had been carried out in a chest clinic by a doctor with wide experience of the procedure. A consultant chest physician said that in his opinion the doctor had used the recognised method in performing the operation. A verdict of death by misadventure was recorded.[1]

Diary of the Week

APRIL 3 TO 9

Tuesday, 5th

ROYAL COLLEGE OF SURGEONS OF ENGLAND Lincoln's Inn Fields W C 2
5 P.M. Mr V E. Negus Comparative Anatomy and Physiology of the Respiratory Tracts in relation to Clinical Problems. (Lister oration.)

Wednesday, 6th

ROYAL SOCIETY OF MEDICINE, 1 Wimpole Street, W 1
5 15 P.M *History of Medicine* Prof. G R. Cameron F.R.S.: Von Kolliker Dr Brice Clarke Katherine Mansfield's Illness
MANCHESTER MEDICAL SOCIETY
4.30 P.M. (Medical School.) *Medicine* Prof. Robert Platt: Life (biological not biographical)

Thursday, 7th

ALFRED ADLER MEDICAL SOCIETY
8 P.M. (11 Chandos Street, W 1) Prof Alexander Kennedy: *Human Reactions to Danger*

Appointments

BOYD T A S, M.B. Glasg F.R.C.S. D.O.M.S part time ophthalmic surgeon, Bangour Hospital, Broxburn West Lothian
CLARKE D M. P R. M.B. N U.I. D.M.R.D radiologist, Mayo county council.
DE WITT W H DE W M.CH.ORTH Lpool F.R.C.S., F R.C.S.I.: orthopædic surgeon, Meath county council
FAIRLEY H BARRIE, M B. Lond., F F.A. R.C.S., D.A.: anæsthetist, Toronto General Hospital and clinical assistant, University of Toronto
HENRY H S A. M.B. Belf. F.R C.S. D.P.H., D.L.O: part time consultant E.N T surgeon South Down and South Armagh group of hospitals.
O'SULLIVAN R. F M.B N U I D.P.H: appointed factory doctor Shelf York.

Birmingham Regional Hospital Board:

ANTON-STEPHENS DEREK M.B Dubl., D P.M. whole-time psychiatrist and deputy medical superintendent Highcroft Hall Hospital
HAWKINS C F., M.D Lond. M R.C.P part time consultant physician, mid Worcestershire group
STROUD M H., M.B. Birm. F.R.C.S: part time consultant E.N.T. surgeon, Birmingham (Dudley Road and West Bromwich groups)
THOMSON J F., M.D Edin. D P.M whole-time consultant child psychiatrist Shrewsbury and Wolverhampton groups
TUDOR, R. W., M.B. Birm, F.R.C.S. whole time senior casualty officer Birmingham (Selly Oak group).
WALSH PETER, L.R.C.P.I. part time asst. [illegible] Wolverhampton group

Manchester Regional Hospital Board:

CHADWICK, D A., M.B. Manc., F.F.A.R.C.S. consultant group anæsthetist, north and mid Cheshire hospital group
CHANDRA, PRAKASH M.B. Lucknow M.CH.ORTH. Lpool, F.R.C.S. senior casualty officer Burnley and district hospitals
CHATTERJEE, S S M.B. Patna, M.R.C.P whole-time asst. chest physician, Baguley Hospital, Manchester
JEWSBURY PERCY M.B. Manc., F.R.C.S. [illegible] surgeon Blackpool and Fylde Hospital [illegible] northern part of the region.
SMITH, A E. M.B. Edin., F.F.A.R.C.S. consultant anæsthetist Bolton and district group of hospitals
TUTTON G K., CH.M. Manc., F.R.C.S. consultant neurosurgeon, Preston and Chorley Hospital Centre and northern part of the region.

Notes and News

MENTAL-HEALTH RESEARCH

The first research fellow to be appointed by the Mental Health Research Fund Dr J D Montagu was presented to those who had gathered at the Mansion House on March 23 to hear more about the fund's future plans. Sir SEYMOUR HOWARD the Lord Mayor spoke of the advances in treatment and prevention of mental ill health which the work of the fund may reasonably hope to forward. Dr W S MACLAY introducing the speakers, mentioned three main lines by which research in this field is at present advancing: by sociological studies of the incidence of mental illness and the like, by studies of the individual by psycho-analysis and allied methods and by studies of an organic nature into the physiology biochemistry and electrophysiology of the brain. For the present, he said the fund is confining its scope to the third of these. Dr DENIS HILL spoke of the light electro-encephalography has already thrown on epilepsy and of its value in locating cerebral tumours. He described cases of epilepsy originating in the temporal lobe which have been treated successfully by removal of the brain area in which the epileptic discharge takes place. In the last four years, he said 50 patients have been treated in this way and results have so far been encouraging over half have been freed from fits and 85% have been greatly helped.

Dr ELIOT SLATER speaking of the genetic aspects of mental disorder recalled that one of the first diseases in which an inherited factor was recognised was a mental disease—Huntington's chorea. Other mental disorders do not give such clear evidence as this but studies of siblings, and especially of uniovular twins, have already shown that genetic factors operate in mental illness. This, he said does not mean we need despair about mental disorders: the inherited factors are of a biochemical nature and presumably will in time be as open to treatment as other disorders of body chemistry. Moreover the mental health of the person depends not only on his heredity but also on his environment and the stresses to which life exposes him. He cited a pair of uniovular twins, one of whom became a criminal while the other led an equally exciting and dangerous life without finding it necessary to turn to crime. Prof. J ELKES spoke of the use of drugs in research and treatment, and the information being gained from studies of hallucinogenic drugs, and also from the effects of 'Sodium amytal' in rousing schizophrenics temporarily from stupor. Through such studies as these, he said we may come in time to detect early mental illness by chemical means, and perhaps to suggest antidotes.

In concluding the meeting Sir GEOFFREY VICKERS said that some might ask what need there was for this fund when the Medical Research Council and the Clinical Research Board already administer funds for research. He thought it wrong, he said, that research in any field should rely for support on a single public source, however well administered. In a voluntary enterprise, such as this fund, interest is canalised and specific made of the commonly encountered problem of the employee who believes, against medical evidence, that his work is undermining his health

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[1] *Liverpool Daily Post*, March [illegible]

The floor above deals with some of the commoner industrial and occupational hazards Posters and drawings bring home the need for simple common sense precautions—e g , the importance of wearing protective goggles in any process involving a risk to the eyes, and the wisdom of making sure that electrical fittings are soundly constructed and regularly inspected Finally, there are some interesting exhibits relating to the factory canteen these demonstrate the folly of guarding the worker against trauma while leaving him exposed, during his lunch hour break, to the more subtle menace of *Salmonella typhimurium*

THE OTHER SIDE OF THE TABLE

APPLICANTS for posts in medicine, as in other professions, are expected to pass an examination for which their training has not specifically prepared them Some bring a native shrewdness to the task, and do well , others, equally well fitted for the post, are defeated by native shyness Not a few, perhaps could learn something to their advantage from *The Intelligent Teacher s Guide to Preferment*,[1] in which a director of education offers advice from the selection committee's side of the table Having dealt with such important details as the candidate's application form and covering letter and his choice of referees the author reminds candidates that though they may be ill at ease at the interview, so also may be the inter viewing committee "The wise candidate makes a swift assessment of the situation and does his best to put the committee at their ease, however many butterflies may be fluttering in his own stomach"

Royal College of Obstetricians and Gynæcologists

Mr Vincent Massey, Governor General of Canada, and Dr George W Corner, of Baltimore, will be admitted to the honorary fellowship of the college on July 22

Prof B P Watson, of Columbia University, New York, has been elected William Meredith Fletcher Shaw lecturer for 1955

South West Metropolitan Region

Chest Diseases Group (Eastern Area)—The inaugural meeting of this group will be held at St James' Hospital, Balham, at 2 30 P M on Saturday, April 23, when Sir Clement Price Thomas will speak on Carcinoma of the Lung

U.S Surgeon-General

Major General Silas B Hays, Army Medical Corps, has been appointed surgeon general of the United States Army, in succession to Major General George E Armstrong, who is retiring

Faculty of Anæsthetists

The seventh anniversary dinner of the faculty was held in the Royal College of Surgeons on March 23 Proposing the toast of The Faculty, Sir Charles Dodds said that the last twenty years had witnessed a revolution in the practice of anæsthesia No longer had patients to undergo the rigours of rag and bottle induction or endure the gastro intestinal qualms that followed return to consciousness Thanks to basal anæsthetics, these were things of the past , it was unfortunate, he reflected that some equally effective technique was not available to after dinner speakers to facilitate the descent of their audiences into welcome unconsciousness In reply, Dr Bernard Johnson, the dean spoke of the faculty's responsibilities in the fields of teaching, clinical practice, and research The new anæsthetic research department to be established within the college had been most generously supported by pharmaceutical firms As a result, the faculty would continue to lead the world in the advance of anæsthesia Dr R F Woolmer, vice dean, welcomed the guests in rhyming iambic pentameters—an orthometrical tour de force that provoked enthusiastic applause Replying, Sir Russell Brain disclaimed poetic skill but went on to leave no doubt as to his mastery of prose He noted that anæsthesia, having been the companion of surgery for a century, was now being wooed by medicine Already it had established a place for itself in psychotherapy and there was growing evidence of its value in the treatment of tetanus and bulbar poliomyelitis—facts which proved once again that the more specialised specialties become, the more dependent they are on each other

Queen's Institute of District Nursing

Dr G O Barber is to speak at the conference which this institute is holding at Church House, Westminster, S W 1, on Thursday, May 12, at 2 30 P M , on the Link between Hospital, General Practitioner, and the District Nursing Service

Harveian Society of London

Buckston Browne Prize—The subject chosen for the essays for this prize (£100) for 1956 is Hypertension Entry is open to any doctor, registered in the British Isles or Dominions, who is under 45 years of age Essays must be sent by Aug 31, 1956, to the hon. secretaries of the society, 11, Chandos Street, W 1

Association of Sea and Air Port Health Authorities of the British Isles

The annual general meeting of this association is to take place in London from June 8 to 10 Dr R H Barrott will give a general review of the state of port health administration at the present time, and Dr W D L Smith will speak on Malaria and the Thames

Basingstoke Plastic Centre Medical Society

On Thursday, April 14, at 7 30 P M , at Rooksdown House (Park Prewett Hospital), Basingstoke, Hants, this society will hold a meeting on burns with special reference to the effects of atomic explosions The speakers will include Prof R H. S Thompson, Dr W J Butterfield, Dr P Gorer, Mr Douglas Jackson, and Dr J P Bull

European Rheumatology Congress

This congress is to be held at The Hague from June 13 to 17 The programme is divided into sections on rheumatic fever, connective tissue, osteo arthritis of the spine and disc degeneration, and rheumatism and social medicine Speakers from this country will include Dr E G L Bywaters, Dr L E Glynn, Dr R Consden, and Dr E J Holborow Further particulars may be had from the secretary, Dr H van Swaay, Burg De Monchyplein 9, The Hague, Holland

Welsh National School of Medicine

Dr A Trevor Jones, senior administrative medical officer of the Welsh Regional Hospital Board, is to succeed Prof R M F Picken as provost of the school Professor Picken retires on Sept 30

Dr Jones was educated at the Lewis School, Pengam and he began his medical studies at the University College of South Wales and Monmouthshire in Cardiff before going to University College Hospital London where he qualified in 1924 After spending some years in hospitals in London he returned to Wales in 1929, taking hospital appointments in Swansea and Carmarthen, where he also worked in general practice and became the medical officer of health He was appointed a medical officer on the staff of the Welsh Board of Health in 1935, and during the late war he was the hospital officer for Wales under the Emergency Medical Service Since the start of the National Health Service he has been the senior administrative medical officer to the Welsh Regional Hospital Board He was elected F R C P in 1953 His publications include the report of the survey of the hospital service in South Wales which he carried out in association with Professor Picken and the late Professor Nixon, of Bristol, in 1945

British Society for Research on Ageing

The following honorary officers and members of the executive committee have been elected

Chairman, Sir Charles Dodds, F R S , vice-chairman, Sir Francis Fraser, secretary Mr G H Bourne D SC (London Hospital Medical College London E 1) treasurer Prof P L Krohn, members of committee, Prof J F Danielli D SC , Miss H B Fell, F R.S Prof K J Franklin F R S , Prof P B Medawar, F R.S., Prof R E Tunbridge

Current Conceptions of Allergy

The Society for Visiting Scientists is to hold a meeting on this subject at 5, Old Burlington Street, London, W 1, on Wednesday, April 6, at 7 30 P M Sir Henry Dale, O M , F.R S., will be in the chair and the speakers will be Dr Bernard Halpern, director of research at the Centre National de la Recherche Scientifique, Paris, Prof J R Marrack, and Dr J Pepys

Second International Congress of Neuropathology

This congress will be held in London from Sept 12 to 17 The programme includes discussions on the Pathological Basis of Involuntary Movements, the Neurone, the Blood brain Barrier, Malignancy and Classification of Gliomas, and (with the Symposium Neuroradiologicum) Tentorial Herniation of the Uncus Further information may be had from Dr W H McMenemey, Maida Vale Hospital for Nervous Diseases, W 9

The Queen has consented to the title "Royal" being given to the Australian Flying Doctor Service

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[1] R Rose London Chatto & Windus 1954 Pp 96 65

THE URÆMIAS*

G M BULL

M.D Cape Town F R C.P

ROFESSOR OF MEDICINE IN THE QUEEN'S UNIVERSITY, BELFAST

THE word uræmia means urine in the blood and was rst used by Piorry and Lhéritier in 1840 to indicate the toxication resulting from insufficient purification of the lood by the kidneys It is unfortunate that it is such a hort and descriptive word, for it sounds as if it indicates ne definite clinical picture. In fact it does not

In renal failure one may see a very wide variety of ymptoms and signs which even on Piorry's definition, ould be included as uræmic. With improving bio hemical knowledge it has become possible to attribute ome of these to measurable deviations from the normal ody chemistry I shall aim to review some of the rogress in this field and to show how a better under tanding of the pathogenesis of the uræmias may lead to ional treatment

Definition

The uræmias are those states which occur when the kidneys unable to maintain a normal internal environment, d arise when there is an imbalance between the rates of take or production in the body of chemical substances and ir rates of excretion

This definition emphasises three important points

(1) There is no single clinical picture in renal failure

(2) The uræmias arise from an imbalance between intake d renal function—a concept of great importance in treat ent

(3) Uræmia includes those states which arise from failure the kidney to conserve essential substances as well as states e to retention of urinary constituents.

PATHOGENESIS OF SYMPTOMS AND SIGNS IN THE URÆMIAS

Contrary to earlier beliefs the most important sub tances in the genesis of the uræmias are not the organic nd products of nitrogen metabolism but water and lectrolytes.

Some of the uræmias can be attributed to detectable eviations from the normal chemical content of the body, nd can be recognised by clinical and laboratory methods hese will be described first Others remain unexplained nd will be considered more briefly later

Although each uræmia is described as though it were separate entity it should be remembered that mixed varieties are the rule In each case are outlined the mechanisms of production then the clinical recognition, nd finally the laboratory diagnosis

Symptoms and Signs Attributable to Known Biochemical Abnormalities

ACIDÆMIA

Acidæmia develops when the ratio of strong anion to ixed base rises This may occur in renal disease for the ollowing reasons :

1 The intake of anion (particularly chloride phosphate and ulphate) may exceed the capacity of the kidney to excrete it

2. Fixed base may be lost owing to a defect in renal base-paring mechanisms

3 Fixed base may be lost in diarrhœic stools.

The clinical picture is dominated by the deep sighing espiration and thus is accompanied by various degrees of clouding of consciousness progressing to coma [1] Other symptoms frequently occur in acidæmic patients, but whether they are the result of the acidæmia, or due to associated disturbances, is difficult to say The most common accompaniments are restlessness, headache, and nausea and occasionally there is meningism.

The diagnosis is confirmed by determination of the plasma bicarbonate ($-HCO_3$) level which is reduced in metabolic acidæmia This level is similarly reduced in respiratory alkalæmia from hyperventilation, but in this latter the pH is raised, and tetany (overt or latent) can be demonstrated Tetany does not occur in acidæmia, for reasons which are discussed on p 732

Although incorrect in a strict chemical sense, it is convenient to regard the reduction of the plasma bicarbonate level as a deficiency of fixed base in the body even where the cause is the presence of fixed anion in excess. This is so because, in treatment, we have to provide a quantity of strong cation to correct the disturbance Although we sample only the plasma this deficiency of fixed base is found throughout body water—information which is useful in calculating the quantities of base to be given in treatment

ALKALÆMIA

Alkalæmia is rather uncommon in renal failure and here as in other circumstances it is almost always associated with potassium deficiency That potassium deficiency is an important cause has been shown by Orloff et al (1953) The alkalæmia arises in most cases because of vomiting, with its attendant loss to the body of chloride and potassium but it is occasionally seen when there is a very high intake of alkali.

The clinical picture is usually dominated by tetany caused indirectly by a fall in the level of ionised calcium (The reasons for this are discussed on p 732) Some symptoms however, probably arise from the alkalæmia per se these include stupor, headaches and changes in temperament—or even psychosis Some patients notice a dislike of sweet foods

Estimation of the plasma-HCO_3 level confirms the diagnosis. A rise in $-HCO_3$ is found in metabolic alkalosis, *but also* in *respiratory acidosis* To distinguish between these two we may estimate the blood pH but in practice this is unnecessary because in metabolic alkalosis there is *tetany (latent or overt)* and in respiratory acidosis there is central cyanosis

HYPERPOTASSÆMIA

Little is known of the rôle of changes in cellular potassium content in renal failure and the main clinical importance of the potassium ion is that changes in its concentration in extracellular fluid sometimes give rise to symptoms and signs, and may cause death Hyper potassæmia occurs in the following circumstances :

(1) Potassium intake may exceed the capacity of the kidney to excrete it The reprehensible practice of administering potassium citrate as a diuretic in acute nephritis, and its routine administration to all patients receiving sulphonamides must have caused many fatalities in this way

(2) Potassium may be released from its protein binding in cells during katabolism and then migrate into the extracellular space This occurs particularly when the rate of katabolism is high as in anuric patients receiving too few calories in the diet and in those with infections It also occurs in underhydrated patients. Here the reason is probably as shown in fig 1 This variety of hyperpotassæmia may be seen even in the presence of a deficiency of potassium in the body as a whole and it is almost always seen in extracellular underhydration.

It is unfortunate that in most patients there are no presenting symptoms and signs of hyperpotassæmia. The patient dies suddenly of cardiac arrest Very rarely indeed, hyperpotassæmia may be accompanied by a flaccid hyporeflexic generalised paralysis, clinically indistinguishable from that which may occur with hypopotassæmia We certainly cannot afford to await the development of paralysis, and the diagnosis of hyperpotassæmia must be suspected from the attendant circumstances, and confirmed by estimating the serum-potassium level Where this is not possible, an electrocardiogram may be of assistance, because a very rough correlation exists between the serum-potassium level and the electrocardiographic pattern

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* The Goulstonian lectures for 1955 delivered before the Royal College of Physicians of London on Jan. 18 and 20 Based on work done with Dr A M Joekes Dr K G Lowe and Miss B M Evans at the Postgraduate Medical School of London and with Dr R N Beck Dr R A Womersley and Miss E Martin at Queen's University and Royal Victoria Hospital Belfast

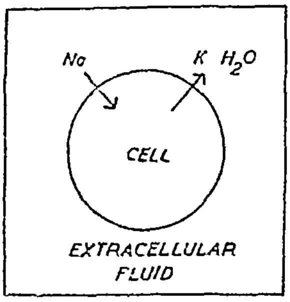

Fig 1—Effect of lowering partial pressure of oxygen on cell water, sodium, and potassium

The oligæmia resulting from underhydration causes a reduction in the general circulation, which in turn causes a fall in partial pressure of oxygen in the tissues and a reduction in renal function—circulatory renal insufficiency When the partial pressure of oxygen falls, potassium is released from the cells and passes into the extracellular fluid (Mudge 1951, Robinson 1953), where its concentration increases, because its excretion is impaired by the circulatory renal insufficiency

POTASSIUM DEFICIENCY

A deficiency of potassium arises when there is a combination of a low intake of the ion with excessive loss either through the kidney or through the gut It is seen characteristically in the following circumstances

(1) In the early diuretic phase of tubular necrosis, where it is presumably due to a defect in tubular reabsorption of potassium (Bull et al 1950)

(2) The same type of defect may be seen rarely in chronic renal disease (Bickel et al 1953, Brown et al 1944, Evans and Milne 1954)

(3) Potassium deficiency also arises because of loss of the ion, in excess of intake, in vomitus or in diarrhœic stools, both of which contain considerable quantities of potassium

Clinically, the hallmark of hypopotassæmia is a flaccid areflexic paralysis, indistinguishable, on neurological examination, from family periodic paralysis However, gross deficiencies of potassium may occur without this paralysis Usually in potassium-deficient patients there is some clouding of consciousness, but whether this is due to potassium lack or to associated disturbances is uncertain

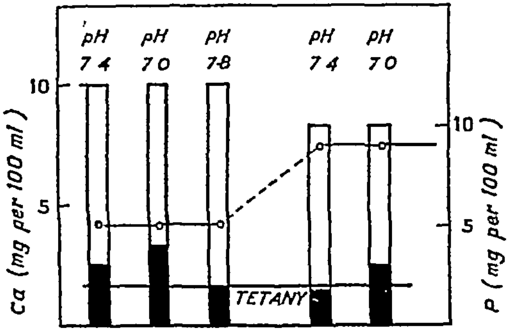

Fig 2—Effect of pH and serum-phosphate level on plasma-ionised calcium level

The proportion of total serum calcium level due to ionised calcium is shown in black In acidæmic patients (as in columns 2 and 5) the proportion ionised increases, and in alkalæmic patients (as in column 3) it decreases.

A rise in serum phosphate level above the normal (as in columns 4 and 5) is associated with a reciprocal fall in serum calcium level At a normal pH this may cause tetany, but 5 shows how acidæmia prevents the development of raising the proportion of calcium ionised.

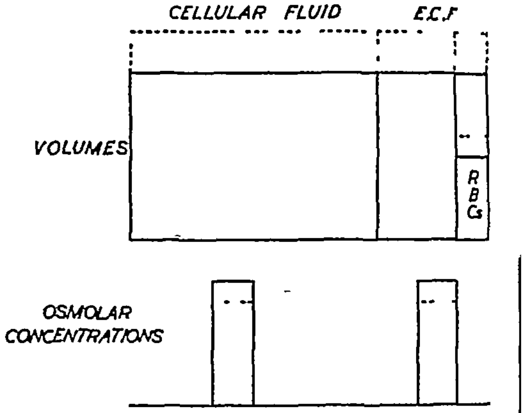

Fig 3—Cellular and extracellular overhydration

For comment, see text In this and subsequent simil figures the solid line represents the normal, and the dott line the abnormal

The diagnosis may be confirmed by determining th serum potassium level or by electrocardiography Unfortunately I do not know of any simple method of estimating quantitatively the extent of the deficiency of potassiu in the body as a whole

DISTURBANCES IN CALCIUM LEVEL

The level of ionisable calcium in the extracellul fluid may be altered in renal failure The most importa causes of these alterations are changes in the plasma p and the plasma inorganic phosphate concentration Their effect is shown in fig 2

The serum-inorganic phosphate level rises in parall with azotæmia when the glomerular filtration-rate reduced Secondary to this, there is a fall in level of serum calcium

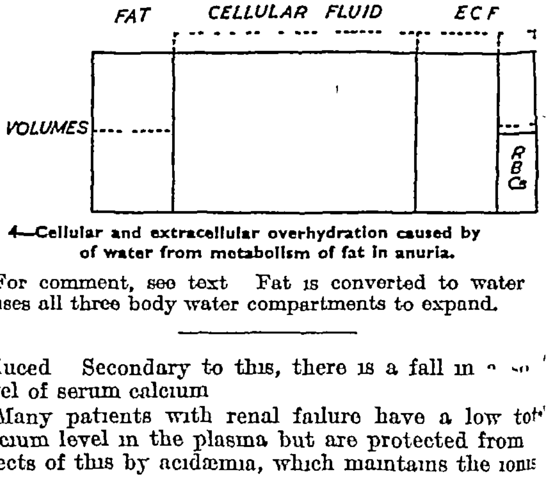

Fig 4—Cellular and extracellular overhydration caused by of water from metabolism of fat in anuria.

For comment, see text Fat is converted to water causes all three body water compartments to expand.

Many patients with renal failure have a low tot calcium level in the plasma but are protected from effects of this by acidæmia, which maintains the ionis fraction at near normal levels If the acidæmia corrected without a fall in the inorganic phosphate of plasma, they develop tetany Lowering of the level ionised calcium is one of the causes, though not a co one, of twitching and generalised epileptiform conv in renal failure

Hypercalcæmia is very uncommon in renal failure, where it occurs it is usually the cause rather than result of the failure, as in vitamin-D int sarcoidosis, hyperparathyroidism, and myelomatosis

DISTURBANCES OF MAGNESIUM CONTENT OF THE B

Hypermagnesæmia occurs occasionally in renal fail when the intake of the ion is particularly high and rate of excretion low It is usually the sequel to ad tration of magnesium sulphate as an aperient T

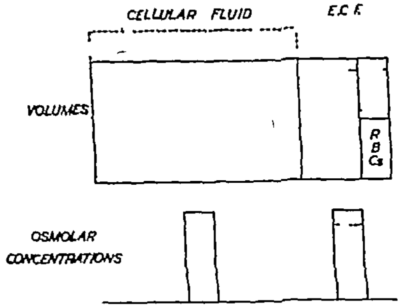

Fig 5—Cellular overhydration due to decreased extracellular osmolarity

For comment, see text

clinical effect is the same as the administration of a sedative

Magnesium deficiency is found in the early diuretic phase of acute tubular necrosis, but no clinical picture can yet be attributed to it with certainty

DISTURBANCES OF WATER BALANCE

Last among the known disturbances considered are those affecting water balance These are less well known than the others but of greater importance. They probably cause more deaths than all the others combined

Four types may be recognised—cellular overhydration and underhydration and extracellular overhydration and underhydration—and various combinations of these occur

Cellular Overhydration

Cellular overhydration is a common disturbance It occurs especially in the anurias but it may also be seen in chronic renal failure and in certain types of circulatory renal insufficiency The main factors determining its occurrence are (1) a discrepancy between intake and output of water and (2) the osmotic pressure of the body fluids, which is in turn affected by intake and output of electrolyte

The following examples illustrate how these factors operate:

The fluid intake or the rate of production of water from fat, carbohydrate and protein may exceed the rate of fluid loss from the body, leading to an expansion of all body water compartments and a fall in the concentration of their solutes (fig 3) This is commonly seen in the anurias. When the rate of water intake is very high, patients with chronic renal failure may develop cellular overhydration by this same mechanism

I once had a patient with chronic renal failure who unwisely drank 5 litres of water in about an hour He became nauseated and confused very soon afterwards. His volume of urine increased sharply for about half an hour and then decreased to oliguric levels. He died about four hours later

Funck Brentano (1953) has studied this phenomenon of oliguria in cellular overhydration and believes that swelling of renal cells may account for the deterioration in renal function. Even if this explanation is incorrect, it is important to recognise that cellular overhydration is dangerous for this reason as well as for others.

In treating anuric patients it seems at first sight that by keeping the total body weight constant we could avoid overhydration. Hamburger and Mathé (1954) point out that this is not so, because the katabolism of fat and tissue releases water which enters the fluid compartments of the body and so alters the ratio of dry weight to total weight. Each gramme of fat burnt releases about 1·25 ml. of water The mechanism is illustrated in fig 4

The osmolarity of extracellular fluid may fall and allow water to diffuse into the cells (fig 5) Na and Cl are the commonest extracellular ions and contribute most of the osmotic pressure of extracellular fluid If for any reason the concentration of these ions, especially Na ion, is low, the osmolarity of the extracellular fluid decreases, and water tends to move along an osmotic gradient into the cells, until osmotic equilibrium has been regained

The sodium content of the body may be low because of reduced intake, as in patients on low-salt diets, but the usual cause is undue loss of the ion. This may take place through diarrhœa, vomiting, or sweating, or, most important, through the kidney This renal loss of Na is of special importance because it occurs very commonly in both acute renal failure (Bull et al. 1950) and chronic renal failure (Nickel et al 1953) Fig 6 shows how extensive the loss may be in acute tubular necrosis and fig 7 in chronic renal failure.

In my experience, this uncontrolled salt loss is invariable in the early diuretic phase of acute tubular necrosis. In chronic renal disease it is also very common I believe that it occurs to some extent in nearly 50% of patients, although it is rare in the gross form described by Thorn et al (1944) which simulates Addison's disease.

Mechanism of salt wasting.—There are two main reasons for loss of salt in renal disease.

(1) If, in a normal person, we induce an osmotic diuresis—e.g., by injection of mannitol or by ingestion of urea—the volume of urine increases and with it the excretion of Na (figs 8 and 9)

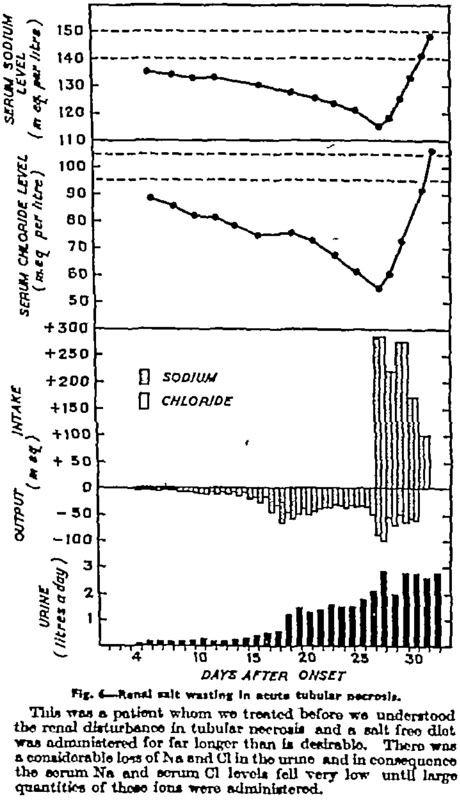

Fig. 6—Renal salt wasting in acute tubular necrosis.

This was a patient whom we treated before we understood the renal disturbance in tubular necrosis and a salt free diet was administered for far longer than is desirable. There was a considerable loss of Na and Cl in the urine and in consequence the serum Na and serum Cl levels fell very low until large quantities of these ions were administered.

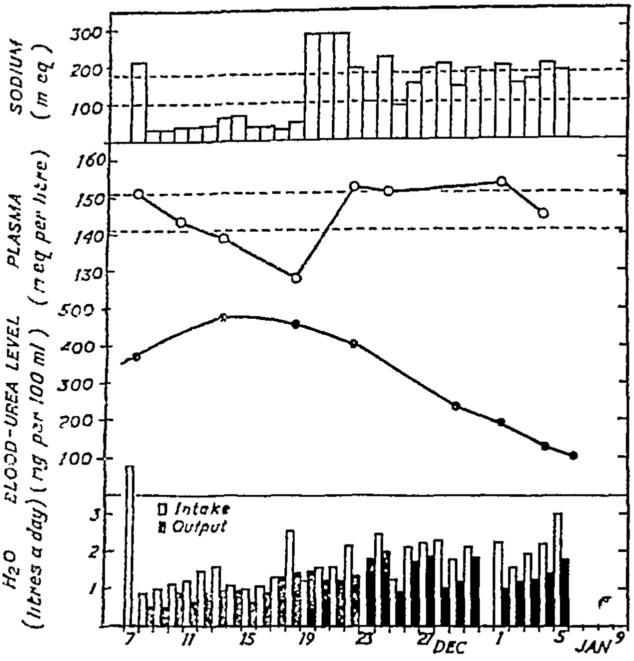

Fig 7—Salt wasting in a patient with chronic renal failure.

The figure shows sodium wasting in a patient with chronic renal failure Between Dec 7 and 19 the serum sodium level fell well below the normal range despite an intake of sodium of about 50 m eq a day, equivalent to an intake of about 3 g of salt per day A normal person can maintain salt balance on an intake of a tenth of this To maintain balance a large intake of sodium (about 200 m eq per day) was required

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It has been shown by Rapoport et al (1949) that the change in excretion of Na and H_2O can be directly correlated with the excreted load—i e, the number of mols of solute excreted in the urine—and is independent of the type of solute

Where the number of nephrons is reduced and the excreted load kept constant, the load per nephron is increased, and this has the same effect as a high over-all load in a normal person

Thus, a patient with renal disease, in balance on an ordinary diet, excretes per minute the same amount of urea and other osmotically active solutes as a normal person, but through fewer nephrons The excreted load per nephron is therefore higher than normal, and these patients are, in fact, in a constant state of osmotic diuresis They excrete more Na than they should, and have a constant polyuria. As Fremont-Smith et al (1931), Homer Smith (1951), and Platt (1950) point out, this osmotic diuresis may also explain the isosthenuria of renal failure, for the following reason

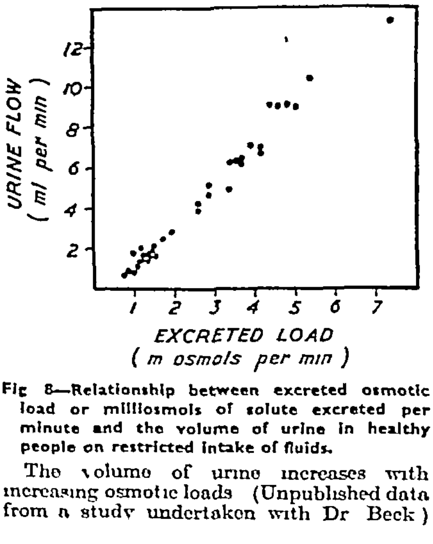


Fig 8—Relationship between excreted osmotic load or milliosmols of solute excreted per minute and the volume of urine in healthy people on restricted intake of fluids.

The volume of urine increases with increasing osmotic loads (Unpublished data from a study undertaken with Dr Beck)

If we administer an osmotic load to a hydropenic patient excreting concentrated u we find, in addition to a diuresis, a decrease in the of the urine towards that of the plasma, which is about 3 milliosmols per litre Similarly, an osmotic load in an o hydrated patient passing dilute urine increases the osmolari of the urine (fig 10)

As the osmolarity and the specific gravity of the urine approximately correlated, it is easy to see how an osmotic load, even in a normal person, contracts the possi range of specific gravity of the urine, until eventually becomes fixed at 1 010, or 310 milliosmols per litre In re disease the same effect is brought about by a reduction in number of nephrons

(2) Another reason for the Na loss in renal failure i that, where the base-sparing capacity of the kidney reduced, as in renal failure, fixed base, particularly Na, is excreted in increased amounts when the patient is acidotic As most diets are acidifying, this becomes a factor in increasing the drain of Na from the body Isolated abnormalities of the tubules exist in which it is the only cause of Na wasting

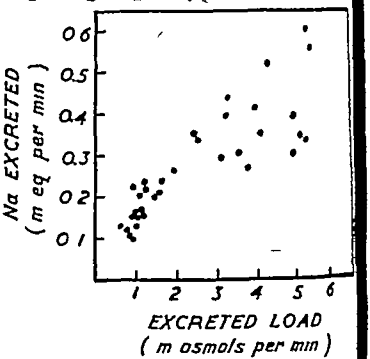


Fig 9—Relationship between excreted osmo tic load or milliosmols of solute excre per minute and the urinary excretion Na by normal persons

The excretion of Na increases wi increasing osmotic load (Unpublish data from a study undertaken wi Dr Beck)

Clinical recognition of cellular overhydration—The presence of cellular overhydration may be suspected when the history and examination suggest any of the circumstanc mentioned The symptoms and signs of cellular over hydration (modified from Hamburger et al 1950) ar as follows

Clinical

- Anorexia
- Nausea
- Vomiting
- Lassitude
- Stupor and confusion
- Changes of mood
- Coma
- Epileptiform convulsions
- Muscle cramps (unusual)

Laboratory

- Low serum Na level
- Low mean corpuscular Hb concentration and high corpuscular volume

Note that the first five of these may aggravate t condition by diminishing Na intake or by increasing loss

Laboratory tests which assist the diagnosis include t determination of the plasma Na level, which is low the mean corpuscular hæmoglobin concentration, is low , and the mean corpuscular volume, which is

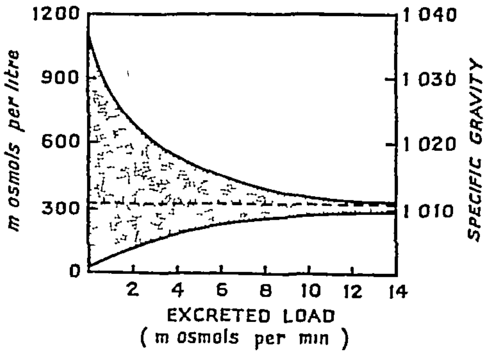
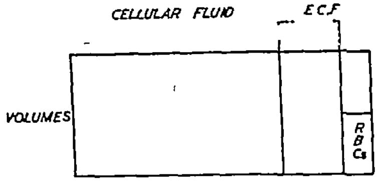


Fig 10—Effect of osmotic load on concentration and dilution of



g 11—Expansion of extracellular space without increase in volume of plasma.

ecause the red cells, in common with other body cells, re overhydrated

A low value for the plasma Na level is not patho nomonic of cellular overhydration, and can occur with ormal cell hydration in nephrosis and other protein eficiency states.

xtracellular Overhydration

Two varieties can be distinguished

Pure expansion of extracellular space without increase n volume of the plasma (fig 11)—e.g., nephrosis Here he symptoms and signs are those of the œdema alone

Expansion of extracellular space with increase in plasma volume (fig 12)—This is more serious. It occurs in ongestive heart-failure, following excessive administra ion of adrenocortical hormones and in renal disease when water and salt are given in excess of the ability of the idney to excrete them A good example of the last type is in anuric patients given excessive quantities of intra venous saline solution or of sodium sulphate. The symptoms and signs are those of congestive cardiac failure Here it should be pointed out that the heart failure itself reduces renal function further and lessens the ability of the kidney to correct the imbalance.

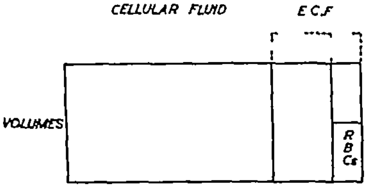


Fig. 12—Expansion of extracellular space with increase in volume of plasma.

The condition is recognised from the history and physical examination, with special reference to observa tion of the venous pressure The specific gravity of the plasma is usually low

Cellular Underhydration

Cellular underhydration occurs when the rate of water intake is less than the rate of loss by all routes. Here cellular and extracellular underhydration usually coexist. In these cases the extent of the underhydration can be roughly assessed by measuring the specific gravity of the plasma. The reason for this is shown in fig 13 Phillips (1950) has shown that for each 0·001 rise in the specific gravity of the plasma above the normal 1 027, the patient lacks about 200 ml. of fluid

Less commonly cellular underhydration may occur with either normal hydration or overhydration of the extracellular space Here the mechanism is a primary retention of Na and an osmotic movement of water towards the extracellular ions takes place (fig 14) The usual cause of this type of cellular underhydration is the administration of isotonic Na containing fluids to ydrated patients without additional water Water is t in the breath and through the skin and in certain cumstances through the kidney also with the result that the extracellular fluid becomes hypertonic and water moves from the cells.

If the patient is conscious he complains of thirst Later he becomes stuporose or comatose, and often he develops coarse twitchings rather like those seen in hepatic coma Particularly in children, the body temperature may rise sometimes to as high as 103°F The tongue is small, and in a severe case the muscles have a curious doughy feel which may be mistaken for œdema. The finding of a high plasma Na level confirms the diagnosis

Extracellular Underhydration

Extracellular underhydration may occur as a part of general under hydration or as an isolated manifestation In the latter case it is due to a deficiency of extracellular ions.

The clinical picture with sunken facies lax skin, diminished eyeball tension and later, hypotension and rapid pulse is well known The measurement of the specific gravity of the plasma is very valuable in assessing the extent of the water lack.

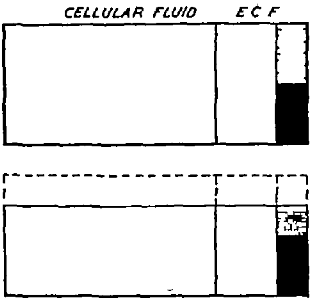


Fig 13—Cellular and extracellular underhydration (illustrating rise in plasma-protein concentration)

The dots represent protein molecules. Their concentration rises as water is lost from the plasma. The specific gravity of protein free plasma is about 1 008, and that of normal whole blood 1 027 The difference between these two figures is due to serum proteins. Therefore the specific gravity of plasma can be used to measure the plasma protein level.

It is particularly important to recognise extracellular underhydration because it leads to peripheral circulatory failure with associated circulatory renal insufficiency (extrarenal uræmia) This secondary reduction in renal function may cause many of the other uræmic pictures already dealt with

Uræmic Manifestations whose Mechanisms are Unknown

Anæmia—Chronic azotæmia is almost always accom panied by a normocytic normochromic anæmia, and the severity of the anæmia parallels that of the azotæmia.

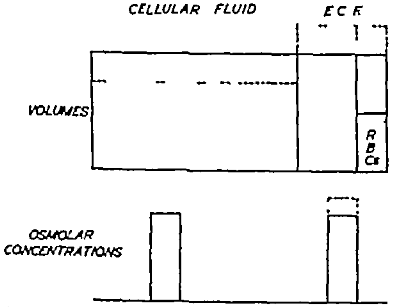


Fig 14—Cellular underhydration due to hypertonicity of extracellular fluid.

For comment see text.

The mechanism is unknown, except that the anæmia is usually of the dyshæmopoietic type but occasionally has a hæmolytic element It does not respond to the usual hæmatinics

Anæmia is important because it may cause cardiac failure or circulatory renal insufficiency, both of which make the azotæmia worse

Purpura is common in terminal uræmic states Again, the mechanism is unknown

Intestinal disturbances—Stomatitis, gastritis, enteritis, and colitis may occur in severe renal failure These may be produced by high concentrations of ammonia formed from urea by the urease normally present in the gastric mucosa and in intestinal organisms

Pericarditis occurs in terminal renal failure No completely satisfactory explanation has been given

Infection is very common in terminal uræmic states and plays an important part in causing death in many patients with renal failure (table I) Such patients appear to be particularly liable to infection, especially bronchopneumonia In some this tendency is obviously explained by a disturbed level of consciousness, but in others there is no obvious cause, and one wonders whether there is some disturbance in the immunity mechanism in the lung Possibly the curious "uræmic œdema" of the lung described by Doniach (1947) acts as a precipitating factor The usual infecting organism is the staphylococcus, and at least in the last few years this has been penicillin resistant in many cases

TABLE I—CAUSES OF DEATH IN RENAL FAILURE

Disease	Infection	Other causes
Acute renal failure * (mostly acute tubular necrosis)	24 (63%)	14
Chronic renal failure †	13 (35%)	24

* Mostly patients seen with Dr Joekes and Dr Lowe

† From necropsy records of department of pathology, Belfast. Figures kindly supplied by Professor Biggart.

Infections are important in two ways they may prove fatal because of the toxæmia, but also they may increase metabolism and so flood the system with end-products of tissue breakdown, disturbing an already precarious state of water and electrolyte balance Release of potassium from cells as a result of this katabolism is of special importance in the anurias

Thus in the management of renal failure the prevention and treatment of infection and its consequences require careful attention

Conclusions

Combinations of the disturbances described account for most of the clinical pictures met with in renal failure, but I do not wish to leave the impression that they account for all Some patients may be comatose or even die without our being able to detect, by our present techniques, any causal chemical abnormality Conversely, other patients may show quite gross deviations from the normal blood chemistry, with no clinical abnormality

(*To be concluded*)

"The theory of the modern kitchen and the labour-saving device is that it suddenly launched women on to new seas of opportunity, oceans of rippling, sun flecked leisure And there is no doubt at all that it has absorbed, via the electric motor, a great deal of absurd drudgery which no human being ought to have to do at all But it now appears that women still have to decide to use wisely the leisure they have gained And the Senate report seems to say that there is still no electronic escape from the time that should be given to children, and no substitute for the maybe seemingly lazy contact with one's own children It is not the male tyrant any longer, or the educator, or the intellectual who insists that woman's place is in the home It is now, heaven help us, the psychiatrist"—ALISTAIR COOKE, *Listener*, March 31, 1955, p 561

THE DIFFICULT APPENDIX

PHYSIOLOGY APPLIED TO DIAGNOSIS

J A. KERR

B Sc Birm, F R C S

CONSULTANT SURGEON, HASTINGS GROUP OF HOSPITALS

TWENTY-FIVE years ago, as a locum in general, I was called to a young girl who complained of intermittent abdominal pain and vomiting Daily observation failed to elicit any physical signs After five days another practitioner was called in, but too late The patient had general peritonitis and died shortly after admission to hospital.

Later, when in general practice on my own account in the country, I saw a young man who had had sudden violent abdominal pain and vomiting There was no abdominal rigidity nor tenderness, but during the course of the day localised deep tenderness in the right iliac fossa was discovered There was no pyrexia and the pulse-rate was 60 A colleague who was called in agreed with my belated diagnosis A backward-lying perforated appendix was removed and the patient recovered.

A few months later, in hospital practice, I saw a boy with no abdominal signs, no pain, no pyrexia, and no rise in pulse rate He appeared to be perfectly well and I was inclined to send him back to his doctor, whose letter recorded abdominal pain and tenderness On the strength of this, however, the boy was admitted Pain and tenderness soon recurred, and three hours after admission a gangrenous appendix was removed and he recovered

Diagnosis

The final diagnosis of appendicitis must be based on the correlation of the pathological changes with the clinical picture—a picture built up from the physical signs and the significant details in the history. The notes made at the time of examination must be continued at the operation by recording the position and external appearance of the appendix, surrounding organs, and peritoneal cavity A specimen of any peritoneal fluid is taken for microscopy, culture, and tests of sensitivity to antibiotics The appendix is slit from end to end and its walls, mucosa, and contents examined A watchmaker's eyeglass may reveal a fascinating vascular pattern and differentiate post-inflammatory petechiæ from vascular flares

The First Attack

The first attack is ushered in by diffuse central or transverse umbilical pain, of gradual onset and steadily increasing severity, and nausea This pain is visceral and is referred along the 10th dorsal nerves, the excitable state of which is shown by Ligat's sign—that is, pain on pinching and drawing away the skin and subcutaneous tissue on one side or the other below the umbilicus Later, abnormal stimulation of the parietal peritoneum may accentuate the spinal reflex on the right side, thus giving the sign as Ligat described it Pain may be epigastric from pylorospasm, or hypogastric from spasm of the sigmoid colon, with loss of appetite, nausea, and vomiting on the one hand and constipation on the other

The inflammation may resolve in a few days and the appendix return apparently to normal It may leave a condition of fibrosis, either diffuse in the walls, or around certain lymph follicles, leading to sunken red petechiæ, which turn purple within a year of the attack, and in course of years may become white, giving a appearance The red hæmorrhagic flares caused by application of forceps to the meso appendix are sunken Recurrent attacks of catarrh presumably the condition of diffuse fibrosis of the wall with mucosa and progressive obliteration of the lumen the tip backwards, leading eventually to a natural On the other hand, fibrosis may lead to localised ig of the lumen with incomplete emptying and stercolith ormation with retention

The first attack may hardly have been noticed by the atient or may have been forgotten Subsequent attacks ay be similar to the first, or may start with pain in the ight lower quadrant, or with nausea or mid abdominal olic due to appendicular obstruction either from œdema omplicating fibrosis of the walls or from impaction of stercolith Continuing obstruction of the lumen is ollowed by distension and gangrene of the mucosa, with pread of the infection through the wall in the case of tricture or local ischæmic necrosis in the case of an mpacted stercolith, which may ulcerate through the vall and into the peritoneal cavity Gangrene or perfora ion gives relief of the visceral pain and disappearance f Ligat's sign Peritonitis may then be diffuse, or imited to a local pocket or to a focal abscess by a cap f greater omentum In the rare case where obstruction s not complicated by infection or gangrene, a mucocele f the appendix is formed

The Position of the Appendix

The effect of the progress of inflammation from the mucosa through the wall to the serous surface depends on the site of the appendix and its relation to surrounding viscera and parietal peritoneum. Irritation is caused by direct contact with the inflamed appendix and by centrifugal spread of irritation in the peritoneal cavity The vehicle of this irritation which may be likened to an odour, is presumably peritoneal fluid exuded from the serosa of the appendix

Should the appendix be lying untethered in what is considered to be the normal position, with maximum tenderness deep to McBurney's point, this irritation has access to the parietal peritoneum, pain is referred by spinal reflex to the right lower quadrant and it is aggravated by spinal or respiratory movements or by any considerable or sudden movement of the abdominal wall with consequent voluntary limitation of these movements and involuntary protective increase in muscle tone of the parietes by spinal reflex Sudden release of pressure gives rebound tenderness and referred tenderness particularly on rebound can be demonstrated by pressure elsewhere Some degree of local ileus is shown by a silent abdomen constipation, and fœtor of the breath Parietal irritation is also accompanied by rise in temperature and pulse rate

The inflamed *paracæcal appendix* gives tenderness on pressure in the outer part of the right loin, and anteriorly $1^{1}/_{2}$ in. above and external to McBurney's point

The rarer *inverted cæcum* gives tenderness over the gall bladder to which the appendix is then adjacent and the diagnosis is made easier by re-examination after hyperextension of the lumbar spine by means of a pillow in the small of the back to separate these organs.

The *retrocæcal appendix* can be considered to be extraperitoneal There is irritation of the cæcum and adjacent muscles with excess of flatus or early transient true diarrhœa, and tenderness in the loin below the right kidney Bimanual examination between the loin and flank may suggest renal tenderness but tenderness is also continued caudally and is not localised to the kidney Direct irritation of the ureter may produce some increase in frequency of micturition which is not, however so marked as in urinary infection It must be realised that urinary infection and appendicitis may co-exist and that removal of the appendix may clear the urinary infection Protective flexion at the right hip joint is produced by psoas irritation there is pain on walking and passive extension of the right hip gives pain in the right lower quadrant or groin (*psoas-stretching test*)

The inflamed *pelvic appendix* may irritate the bladder giving rise to hypogastric pain relieved by micturition the rectum with a discharge of mucus (a spurious diarrhœa) or the lumbosacral cord giving pain referred down the lower limb These symptoms are relieved by appendicectomy The sign of an inflamed pelvic appendix however, is high right posterolateral tenderness and fullness at the finger tip on rectal examination, with pain referred to the abdomen This may be confirmed by pain on passive internal rotation of the right hip in flexion (obturator internus stretching test) Tenderness may also be elicited by deep localised pressure $1^{1}/_{2}$ in below and internal to McBurney's point, this however, may be absent, and I have not commonly elicited the obturator test

The difficult case for diagnosis is the inflamed *tethered retro mesenteric appendix*, which gives none of these parietal signs The only organ directly irritated is the lower ileum with its mesentery The appendix is connected by its meso appendix with the left leaf of the mesentery of the ileum Should this meso-appendix be long the appendix is mobile and is free to irritate the parietal peritoneum by direct contact or centrifugal spread, with local pain and the generally recognised signs of the mobile inflamed appendix.

There is an anatomical variation, however, in which the meso appendix is short near the tip allowing little or no movement between the appendix and the deep surface of the mesentery of the ileum, in which in fact it may be embedded This can effectively enclose the inflamed appendix without help from the greater omentum, beneath the mesentery of the ileum, deep in the coils of small gut, local dilatation of which protects the appendix from the tenderness of ordinary pressure and the parietal peritoneum from irritation Infection is free to spread deep in the left iliac fossa and down to the pelvis still enclosed in mesentery and gut

Pain is not localised to the right lower quadrant There is no muscular rigidity nor increase in muscular tone, no tenderness on light pressure nor guarding no rise in temperature nor marked rise in pulse rate The bowel is not silent, and through absence of constipation there is no fœtor of the breath and the tongue is clean The patient does not look ill, has periods without pain, and may go to sleep

Tenderness if present in these cases, can only be elicited by localised deep pressure with one finger, $1^{1}/_{2}$ in above and internal to McBurney's point—that is, midway between McBurney's point and the umbilicus—and from this point in a vertical line upwards 2 in long with its centre 1 in. to the right of the umbilicus. This deep pressure may produce guarding and tenderness may be more marked on rebound

The inflamed posteriorly fixed appendix is distinguished by the absence of those parietal signs which are found in a mobile organ, and the usual quiet abdomen with constipation is replaced by symptoms of local activity of the bowel the retrocæcal appendix by excess of flatus or true diarrhœa at the onset; the pelvic appendix by spurious diarrhœa; and the tethered retromesenteric appendix by symptoms to be described below

Bowel Symptoms

The tendency to stasis from localised paralytic ileus is countered by direct irritation of the lower ileum. This is revealed by the auscultation of intermittent bursts of squirting borborygmi which may sometimes be continuous, but there is no diarrhœa The patient may say he has diarrhœa, but careful questioning will elicit the fact that the motions are frequent and soft but not fluid Not having been subjected to the action of a laxative the bowels are spontaneously opened three or four times in a day with small formed motions, followed by perhaps one or more soft motions which may be green The ileum propels its contents with increased frequency into the cæcum whence progress along the colon is more leisurely enabling some fluid absorption to take place, though progress is somewhat faster than normal These frequent bowel actions are also described in previous attacks and may last for only one day, local ileus then predominating

Rupture, should it occur, is into the retro mesenteric pocket and there is no generalised " burst spread " Pain and hyperæsthesia disappear, and dilated gut cushions the part from tenderness and the parietal peritoneum from irritation There is a latent interval with no physical signs, *comparable with that of gangrenous* intussusception and of gall stone ileus The bowel is in a state of ileus due to sub-ileal peritonitis No flatus or fæces is passed, and auscultation reveals a silent abdomen Later, deep localised bilateral tenderness is found, and within one to three days nausea recurs with some pain, and bowel actions are resumed These take the form of diarrhœa, from external irritation of the distal large bowel (see cases 1, 2, 4, and 5 below) Nausea ceases and *the tongue is clean Distension* is a feature when ileus is accentuated by the taking of a purge (case 4), when bowel action is delayed (case 3), or where peritonitis is prolonged (case 1)

Illustrative Cases

All these patients were seen by consultants, who found some difficulty in diagnosis Each case seems to show the symptoms and signs which can be expected in the various stages *of an acutely inflamed tethered retro*-mesenteric appendix The most serious and complicated cases come first, and the later ones show progressively less serious complications and earlier diagnosis I have indicated in parenthesis what I consider to be the time of perforation of the appendix

Case 1 General Peritonitis, Mesenteric Phlebitis, Portal Pyæmia

A man of 38 was well until a fortnight before admission, when he had abdominal pain which lasted for a few days (*appendix perforated when pain ceased*) A week after the onset he had diarrhœa and vomiting, thought to be due to gastric influenza Three days later, on a Saturday, he felt ill with abdominal pain and vomiting, some distension and constipation Bowels were moved with aperients On the Sunday and Monday the vomiting continued every six hours or so , it was not fæculent, and he passed a little flatus He was admitted to hospital on the Wednesday with a temperature of 97°F, pulse rate 84, and respirations 20 A plain radiograph of the abdomen showed multiple fluid levels

Operation revealed a gangrenous appendix which had caused general peritonitis The abdomen was mopped out as much as possible and closed with drainage tubes in position There was no postoperative vomiting, but the abdomen became distended Two days after the operation, an intravenous drip was set up and gastric aspiration instituted His temperature rose above normal for the first time since admission. He seemed to do fairly well for a time and was able to drink He passed a small amount of flatus and fæces But a fæcal fistula formed at the lower end of the wound, and he became jaundiced Ten days after admission he was very jaundiced and stuporose, and he collapsed and died that evening

This patient apparently harboured diffuse sub-ileal peritonitis for ten days under careful observation, with *no morning or evening pyrexia for a fortnight* Tenderness was absent or slight and transitory, and no rigidity was found Intestinal obstruction threatened after a week The temperature first registered above normal the day following operation The cause of death was mesenteric thrombosis, fæcal fistula, and portal pyæmia

A colleague has told me of a similar case kept under careful observation in hospital before operation, with similar operative findings, the appendix lying backwards and adjacent to the mesentery of the ileum The patient became jaundiced and died

Case 2 Diffuse Peritonitis, Recurrent Abscesses, Fæcal Fistula

Two years before I first saw her, a girl of 23 had had her first attack of abdominal pain, lasting thirty six or forty eight hours , she felt sick and retched, and there was pain and tenderness around the umbilicus A year later she had a similar attack, and then no further trouble She had a three stage thoracoplasty nearly twelve months before I saw her Two days earlier she ate some cooked cheese, which upset her Next day she felt sick with recurrent periumb soreness which came and went, like an occasional kick in stomach *She felt better in the evening (appendix perf* and on the following morning, but she still had c pain In the evening her temperature was 100 4°F (6 P and 101°F (6 30 P M) She had slight pain and very occa nausea She had taken only a little fluid. The bowels had opened and *no flatus had been passed* but she had had enema that afternoon with flatus result and felt better, she vomited once copiously In this attack, there was exce flatulence with eructation and relief There were no urin symptoms and no rigors She had just finished a peri Previous attacks were not remembered to have had relation to periods

At 8 P M the abdomen was slightly distended. Lig sign was absent There was good but even tone of the abdo nal muscles No superficial nor deep tenderness could elicited, and *there* was no rebound sign The abdomen w silent The rectum was almost empty, but a little balloon with some tenderness referred to the hypogastrium Conclu sion " I must diagnose an inflamed backward lying append here "

A *white cell* count showed *21,000 cells* per c.mm. 9 10 P M , obturator internus and psoas stretching tests w both found to be negative She felt quite comfortable a had slept

Next morning I learned she had vomited bile and had pas *two loose stools* with relief There was very slight deep tende ness on either side below the umbilicus The abdomen w still quiet The white cell count was 30,000 (80% polymorph the temperature 99 2°F, and pulse 112 She was admitt to hospital and operated on in the afternoon An acute inflamed appendix, gangrenous and *perforated at the* ba was removed There was a fæcolith lying free in the periton cavity, and much foul fluid The appendix was lying backw behind the ileo cæcal junction There was no stump appendix because of the perforation The hole in the cæc *was oversewn as well as possible, and the abdomen* drain by one tube

She had a difficult time and did not leave hospital un six months later A pelvic abscess developed, which burst an passed per rectum a month after the operation Three wee *later she had a laparotomy* with *aspiration and* drainage of localised extraperitoneal abscess running from the left ili fossa down to the left side of the pelvis and to the right the midline Four days after this operation fæcal mater and flatus discharged from the wound in the left iliac fos Five weeks later the abscess was drained extraperitoneall by inserting sinus forceps through the wound At a secon drainage six days later a drainage tube was inserted well dow into the cavity ' Lipiodol ' injected into the tube showed narrow track the width of the tube extending about 7 towards the head of the left femur, but no definite cavity month later pain recurred in the left iliac region, and th pelvic abscess had re formed, but this drained satisfactorily and the wound became dry She was left with residu induration in the left iliac fossa Subsequent progress w satisfactory

At various times during her illness, pus from the absc grew coliform bacilli, *Staphylococcus aureus*, and proteus A no time were tubercle bacilli or actinomyces found Th organisms found were sensitive to streptomycin and chlor amphenicol She was given two courses of intraveno aureomycin in the first two months of the illness

When I first saw this patient, she was in the late interval of lower-pole retro-ileal peritonitis after perfora tion of her obstructed appendix Apart from raise temperature and pulse-rate, the only sign was recta tenderness referred to the hypogastrium , the white-ce count was raised, however, and the next morning the was very slight deep bilateral abdominal tenderness.

Case 3 Localised Sub ileal and Pelvic Abscess

A woman aged 73 had severe pains low on both sides of th abdomen with swelling of the abdomen and bad headach For about nine months previously she had had high epigastr pain radiating down the front of the abdomen, not apparentl related to meals, but eased by a light breakfast , it was alwa there, a constant burning pain She had always been const pated, more severely in recent months. She passed sma motions followed by a little blood after straining Pain wok her at night

I first saw her five days after the attack of severe pain She had passed no flatus since (*Appendix had perforated and ileus followed.*) She had vomited a little green bile every day Borborygmi were relieved by eructation There had been pain in the vagina for the past two days. Her bowels had not been open since the attack of pain until the day I saw her when they were opened three times with temporary relief the first time soft the second formed the third a good movement Her temperature was 99·6°F and pulse-rate 84 She was emaciated, with pale eyes. The tongue was clean and dry with a few plaques. The abdomen was resonant distended and tender all over with positive rebound sign There was no true rigidity or palpable tumefaction but I found visible coils of gut with quiet squirting borborygmi in the left lower quadrant No peristalsis was seen The rectum was ballooned and tender She was admitted to hospital with a diagnosis of threatened acute intestinal obstruction probably from carcinoma of the lower colon X ray examination of the abdomen showed some distended coils of small bowel. An enema produced flatus and later a small action

At operation two days after admission, pus was found among the coils of small gut with organised exudate and an abscess deep in the pouch of Douglas. A perforated appendix was adherent to the ileum and it was removed but the stump could not be invaginated Adhesions were separated from the lower end of the ileum Postoperative treatment included half hourly aspiration from an indwelling Ryle's tube intravenous fluid and streptomycin. Two days later flatus was passed and loud squirting borborygmi were heard. Ten days after the operation the abdomen was much distended. The bowel was silent and there was very slow slight visible peristalsis The temperature swung to 102°F Pus discharged spontaneously from the lower end, of the wound and the temperature quickly settled. The patient was discharged fit five weeks after the operation

In this case the peritonitis had not spread but localised to form an abscess among the coils of small gut, and the bowel actions were similar to those to be expected, before perforation from irritation of the lower ileum—that is one soft motion and two formed ones (but see case 5)

Case 4 Localised Abscess Commencing Lower pole Peritonitis

A man aged 67 was admitted to hospital with a diagnosis of subacute intestinal obstruction. His doctor wrote: Three days ago this patient had some indigestion and went off his food Prior to this he had been in great fettle Next day he gave himself a large purge and during the afternoon was smitten with violent abdominal pain. He tried to get to the lavatory but collapsed en route I found him writhing with colic His abdomen was much distended and tight as a drum. Knowing that he has a double rupture I went for his inguinal rings. I thought that I felt a tense swelling high up in the left inguinal canal Before I could be sure he rolled over suddenly and started violent retching, bringing up a little altered blood. When I again examined him there was no swelling in the canal (if there ever had been) and his pain became rapidly better and gr $^{1}/_{144}$ of atropine completed the job (*Appendix perforated.*) I saw him yesterday and he was much better Today he is not so well. He is afebrile with a pulse of 80 and his tongue is dry His lower abdomen is distended His rectum is empty and feels normal He is nauseated but has not been sick He has absolutely no appetite but very little abdominal pain. He has passed several small watery stools but no flatus.

In hospital his temperature was 99°F and pulse rate 84 His eyes were dull and tongue furred brown and dry The abdomen was distended and resonant There was no true rigidity but it had a doughy feel. Ligat's sign was negative. There was slight temporary increased muscle tone in the right lower quadrant. Tinkling sounds were auscultated There was a definite positive rebound sign in the right and left lower quadrants but no referred tenderness. There was slight localised deep tenderness (*a*) 2 in above the pubic tubercle on the left and (*b*) $1^{1}/_{2}$ in. internal to McBurney's point on the right 1 in from the midline and 1 in below the umbilicus. Rectal examination revealed no abnormality A diagnosis of retro ileal appendicitis with lower pole peritonitis was made.

On opening the abdomen red coils of gut were seen but there was no free fluid A backward lying appendix swollen gangrenous, and perforated at the tip was lying in a small abscess cavity with an ounce of thick pus among the coils of small gut A collection of reddish brown fluid was found in the left iliac fossa with a similar collection deep in the pelvis The appendix was removed and the fluid mopped out The upper abdomen was explored with a swab and nothing was found The abscess cavity in the right iliac fossa and the pelvis were both drained Pus from the retro ileal abscess gave a growth of lactose fermenting coliforms. He was given streptomycin (1 g twice daily intramuscularly) with intravenous saline and hourly aspiration of the stomach Next day he was very thirsty and there were no bowel sounds. A week later he looked and felt much better and was on a full diet. His bowels were working his fluid state was good and the abdomen soft Subsequent progress was satisfactory

In this case (and in cases 1 and 2) the diarrhœa was watery and quite transient and, by analogy with case 3, presumably due to direct external irritation of the distal colon and rectum from the spreading peritonitis. This might have remained localised but for the purge which presumably caused early spread of inflammation to the left iliac fossa and to the pelvis, with slight temporary increase in parietal muscle tone, localised bilateral deep tenderness, both direct and on rebound, and distension The temperature rose only slightly above normal just before operation presumably from pus under pressure with pulse rate 84 There was no rigidity After operation, some degree of paralytic ileus persisted for a week. Case 3 with an abscess deep in the coils of small gut showed similar signs and postoperative course

Case 5 Localised Abscess Small-gut Obstruction

A fortnight before I saw her a woman of over 70 had had vomiting and diarrhœa. She took to her bed and the vomiting ceased (*appendix perforated*) and later the diarrhœa stopped too The day before I saw her she took food but later the vomiting recurred with acute abdominal colic Her bowels were open once One of her dogs at the time had symptoms of gastro-enteritis.

We found her temperature 96°F and pulse rate 75 The tongue was clean moist, and red She was having recurrent attacks of supra-umbilical pain. There was a firm or hard tender intra abdominal swelling deep to McBurney's point It was not freely mobile Some borborygmi were heard Rectal examination revealed a fixed cervix and a considerable amount of soft fæces, The vomit was brown and offensive

The patient said that forty years ago she had had a similar pain with gastritis and dysentery recurring one year ago for two or three days. She felt that if she could get her bowels open she would be better She was admitted to hospital and an enema gave a fair result of formed fæces with flatus. The vomiting continued We found shifting dullness in the flanks A diagnosis of acute lower small gut obstruction was made

At operation we drained a fibrotic appendix abscess causing small gut obstruction by adhesions. These were divided leaving some narrowing of the lower ileum. The appendix was removed and a side to-side anastomosis of the lower ileum was constructed A tear in the cæcum was repaired Postoperative progress was satisfactory

Pus from the appendix abscess showed numerous gram negative bacilli and a fair number of gram positive cocci. Culture grew lactose fermenting coliform bacilli and staphylococci overgrown by proteus.

This case, though with a similar localised abscess to case 3 showed persistent diarrhœa for a fortnight This may have been due to enteritis secondary to the small gut obstruction which became acute or the patient may have suffered from the same infection as her dog

Case 6 Gangrenous Appendix

A middle-aged woman was seen in consultation. Three years ago she had had infective hepatitis with severe jaundice for some weeks, and she had had irregular indigestion since then At 2 P.M on the previous day a steady constant stomach ache began but she did not vomit She passed three motions up to 9 P M which were not loose Her temperature and pulse were normal. The tongue was dirty She was seen by a colleague who found generalised abdominal tenderness a little more on the right than on the left. There was no guarding nor rebound tenderness, but she did not like deep pressure Vaginal examination revealed no abnormality and no referred pain. The small-gut was thought to be the seat of the trouble The pain continued all night and the next morning the temperature was 99°F and pulse 96. She vomited a small amount at 10 A M , and passed a motion which was green and black She was now a little more tender all over There was no distension but a little indefinite guarding She had had nothing to eat since the onset of the pain, and a morning cup of tea was recently vomited

When I saw her the tongue was furred, greenish, and moist The abdomen moved with respiration with a catch of severe pain on coughing There was no rigidity or tumefaction She had generalised abdominal tenderness with much rebound tenderness in the right iliac fossa, but no particular pressure tenderness except in the right iliac fossa, maximum at McBurney s point and towards the umbilicus The abdomen was silent Ligat's sign was not elicited, and the obturator-internus test negative Passive hyperextension of the right hip referred pain to the abdomen

Operation revealed an acutely inflamed, green, distended retro mesenteric appendix with white external exudate This was removed and the abdomen closed without drainage Convalescence was uneventful

The appendix lumen contained liquid fæces The mucosa was thin and red with small black patches A fæcal concretion was wedged in the proximal end.

Case 7 Acutely Inflamed Appendix

A child of 7 was admitted after three days' intermittent abdominal pain On the day it began her bowels were moved three times At 4 P M on the day of admission she vomited. Her temperature was then subnormal and pulse rate 88 No tenderness was found in the abdomen or rectum, but scybala were felt Pain and vomiting continued, the pain was mostly around the umbilicus The pulse rate rose to 120 The only abnormal sign which had been elicited was a rising pulse-rate, and on this she was sent to hospital

On admission at 10 40 P.M her temperature was 100°F, and pulse 140 There was guarding on the right side, but she was not particularly tender I saw her at 11 25 P M , when there was good tone of the abdominal muscles, slightly increased in the right lower quadrant, but no tenderness A mobile tumour as big as a hazel nut and like a gland was felt in the right iliac fossa Continuous borborygmi were auscultated Rectal examination revealed tenderness mainly on the right, with pain referred to the umbilicus There was no spontaneous pain

I was uneasily inclined to observe the case as one of gastro-enteritis, but perusal of the case sheet and confident prompting of a wise house surgeon led to immediate operation Through a midline incision a low lying retro ileal appendix with omentum adherent to the bulbous tip was removed There was no free fluid The bulbous tip was found to contain pus, and the mucosa was black Proximal fibrosis closed the cavity Progress was satisfactory

Conclusions

The inflamed tethered retro-mesenteric appendix is deep in the centre of the abdomen, and the symptoms and signs to which it gives rise are entirely visceral from inflammation of the appendix itself and from irritation of the adjacent lower ileum, producing frequent formed motions Tenderness is to be elicited only by localised deep pressure at the sub-ileal point, which in the adult is $1^1/_2$ in from the umbilicus to the right and below, and by pressure in a vertical line extending upwards from this point to 1 in above the level of the umbilicus

Perforation is accompanied by cessation of symptoms and disappearance of subcuticular hyperæsthesia, and peritonitis spreads deep in the left iliac fossa and down to the pelvis, irritating the distal large bowel and giving rise to watery diarrhœa There may then be bilateral deep suprapubic and rectal tenderness

There is no irritation of the parietal peritoneum or greater omentum (and consequently no rise in temperature nor increase in pulse rate of more than 20 beats per minute), no increase in parietal muscular tone, no rigidity, no constipation, and no fœtor of the breath, and the tongue is clean

In the case of the mobile untethered inflamed appendix, nervous reflex from irritation of the parietal peritoneum is the cause of (1) pain in the right lower quadrant, (2) decreased mobility of the abdominal wall, (3) the presence of Ligat's sign on the right side, (4) local increase of muscular tone and rigidity, (5) tend light pressure, (6) referred tenderness, (7) cont of general intestinal stasis with quiet abdomen fœtor of the breath, (8) pyrexia, (9) a rise in pulse of more than 20 beats per minute, (10) con malaise, and (11) sleeplessness

None of these signs is present in the tethered mesenteric appendix, even after rupture with Pus contained under pressure, however, may pyrexia The absence of tenderness to ordinary palpati is explained by localised distension of the lower ileu which can be shown by plain X-ray examination, a by the inaccessibility to pelvic examination when th appendix is both high and unruptured The peritoni can spread quietly *among the coils of small gut* down to the pelvis because the containing power of th greater omentum is elsewhere

Inflammation in the mobile appendix and in th tethered retro mesenteric appendix must be regard *as two different diseases affecting different parts* of th abdominal cavity which are separated by the mesent of the ileum The one has access to the parietal peritone and the general peritoneal cavity, the other is shut behind the mesentery and may spread to the left down to the pelvis, but it may give rise to one upp abdominal complication—mesenteric phlebitis and port pyæmia The symptoms of retro mesenteric appendici are entirely visceral

Summary

The symptoms and signs of the various stages of acu inflammation of the tethered retro-mesenteric appendi are analysed and correlated with the pathological chang

The clinical picture is entirely different from that the inflamed untethered mobile appendix, apart fro the onset of the first attack in the latter before th parietal peritoneum has been irritated The physiologic cause of this difference is indicated

The symptoms and signs of the tethered retro mese teric inflamed appendix *give a changing* picture whi suggests in turn both gastro enteritis and intestin obstruction but is typical of neither Their very pecul arity and alternations, however, paint a clinical pictu of intestinal paralysis interrupted by bursts of ove *activity which do not appear to be adequately reflecte* in the bowel actions This is typical of the condition its various stages

I have regarded McBurney's point as $^1/_2$ in below th midpoint of the line joining the umbilicus to the righ *anterior superior iliac spine*

I wish to thank my colleagues of the Hastings group fo their coöperation. The surgeons have been extremely helpful and my particular interest in the condition was first arous by Dr A F W Hall *The Early Diagnosis of the Acute Abdomen* by Sir Zachary Cope has been worth its weight in gold

IRON-DEFICIENCY ANÆMIA IN PREGNANCY

P B B GATENBY
B.A , M.D Dubl , M R C.P , M.R C P I
VISITING PHYSICIAN, ROTUNDA HOSPITAL , HONORAR
PHYSICIAN, DR STEEVENS' HOSPITAL, DUBLIN

E W LILLIE *
M D Dubl
LATE RESEARCH FELLOW, ROTUNDA HOSPITAL

OUR investigation of the anæmias of pregnanc undertaken at the Rotunda Hospital, Dublin, wi Dr H C Moore, has already been published (Lillie et al 1954, Moore et al 1955) Here we deal with the case of iron deficiency studied at that time

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* In receipt of a grant from the Medical Research Council of Ir

Methods

Blood was taken, for hæmoglobin and hæmatocrit estimation, from every woman *on her first attendance* at the antenatal clinic. At first all women with hæmoglobin below 10 g per 100 ml. were referred to a special anæmia clinic, but the numbers were such that this arrangement had to be revised, and for most of the year only women with hæmoglobin below 9 g were directed to the special clinic

At this clinic the history and examination were noted on a special form Spontaneous symptoms were recorded, and each patient was questioned about personal symptoms, diet and past history Every patient was examined in a similar fashion A particular note was taken of her general appearance the state of the finger nails, and the colour of the tongue and conjunctivæ The heart lungs, and reflexes were examined in all cases. The clinical signs were recorded always by the same observer (P B B G) to avoid error

TABLE I—MONTHLY INCIDENCE OF ANÆMIA IN PREGNANCY

Month	No of pregnancies	No with Hb less than 10 g per 100 ml	No with Hb less than 9 g per 100 ml.
January	389	129 (33%)	54 (14%)
February	428	124 (29%)	54 (13%)
March	358	95 (24%)	40 (10%)
April	312	74 (24%)	36 (12%)
May	370	97 (26%)	39 (11%)
June	356	107 (30%)	32 (9%)
July	348	79 (23%)	25 (7%)
August	379	60 (16%)	20 (5%)
September	363	56 (15%)	14 (4%)
October	383	96 (25%)	33 (9%)
November	340	55 (16%)	19 (6%)
December	237	55 (23%)	23 (10%)
Total	4314	1027 (24%)	389 (9%)

Iron by mouth was prescribed and each patient was seen regularly to make sure that she was taking the drug as ordered. Her blood was examined every four weeks, and she was followed through pregnancy to term. Women who did not respond to oral iron were treated with intravenous iron and, if this did not increase their hæmoglobin their sternal marrow was examined.

Prevalence and Grades of Anæmia

Of 4314 patients 1027 had a hæmoglobin value of less than 10 g per 100 ml If the standard of 10 g be accepted as the lowest value which can be regarded as due to hydræmia (Dieckmann and Wegner 1934), there were 1027 cases of anæmia among the first attendances at the antenatal clinic in the year (23 8% of the pregnant women attending the hospital) Many who had a normal hæmoglobin value on their first attendance became anæmic later in their pregnancy Hence the total incidence of anæmia in pregnancy must be greater than 23 8%

TABLE II—INCIDENCE OF DIFFERENT GRADES OF ANÆMIA

Hb (g per 100 ml)	No. of cases
5·0–5 9	9 (2 25%)
6·0–6 9	22 (5 5%)
7·0–7·9	87 (22 0%)
8·0–8 9	219 (55 0%)
9·0–9·9	60 (15·0%)
Total	397

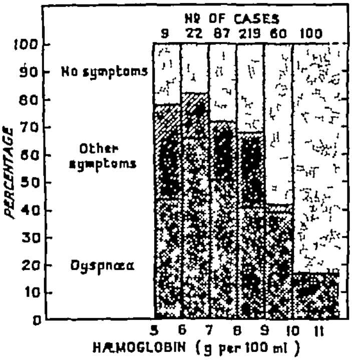

Fig 1—Relation of symptoms to amount of hæmoglobin.

Doyle and McGrath (1954) in a similar survey from the Coombe Hospital, Dublin found an incidence of 31·4% with Hb below 10 g

Dieckmann (1945) found 13% of women at the Chicago Lying in Hospital to have Hb below 10 g

The figure given by Scott and Govan (1949) for Glasgow was 17 6% which they regarded as much higher than those found elsewhere in Britain.

Benstead and Theobald (1952) reported from Bradford that 6 5% of a consecutive series of 2000 women had Hb less than 10 g

Lund (1951) found 20% of 4015 pregnant women attending Charity Hospital, New Orleans, to have Hb below that level.

TABLE III—INCIDENCE OF SYMPTOMS OF ANÆMIA

No of cases	397
No with symptoms	261 (66%)
No without symptoms	136 (34%)
Incidence of symptoms	
Breathlessness	182 (46%)
Tiredness	88 (22%)
Loss of appetite	42 (10%)
Epistaxis	25 (6%)
Headache	17 (4%)
Vomiting	15 (4%)
Sore tongue	6 (1 5%)
Œdema	5 (1%)

The incidence of anæmia seen at the Rotunda Hospital varied according to the season, being lower in the late summer and the autumn (table I) This tendency was also noted by Doyle and McGrath (1954) Similarly Scott and Govan (1940) found that the average monthly hæmoglobin readings in 1946 and 1947 rose in the summer and fell in the winter

From among the 4314 patients investigated, 397 cases of anæmia were studied in detail in the special clinic Table II shows the grades of anæmia found in them The number of cases noted here with hæmoglobin between 9 0 and 9 9 g per 100 ml. is not related to the true prevalence of this grade for many cases in this group were not referred to the special anæmia clinic However, it can be seen that in most of these 397 cases the hæmoglobin lay between 7 g and 9 g As will be shown later, even anæmia of this degree can often be missed clinically

Symptoms

A third of the anæmia patients studied had no symptoms indicating anæmia The order of frequency of

TABLE IV—RELATION OF SYMPTOMS TO HÆMOGLOBIN LEVEL

Hb (g per 100 ml)	No of cases	No symptoms	Dyspnœa	Tiredness	Anorexia	Epistaxis	Headache
9·0–9·9	60	35 (58%)	24 (40%)	11 (18%)	7 (12%)	6 (10%)	2 (3%)
8·0–8 9	219	70 (32%)	90 (41%)	54 (25%)	17 (8%)	8 (4%)	10 (4%)
7·0–7·9	87	25 (28%)	45 (51%)	15 (17%)	11 (13%)	6 (7%)	5 (6%)
6·0–6·9	22	4 (18%)	15 (68%)	6 (27%)	5 (23%)	2 (10%)	0
5·0–5 9	9	2 (22%)	4 (44%)	2 (22%)	1 (10%)	1 (10%)	0

TABLE V—CLINICAL SIGNS OF ANÆMIA IN RELATION TO HB

Hb (g per 100 ml)	No of cases	No signs	With signs
5 0–5 9	9	0	9
6 0–6 9	21	6	15
7 0–9 5	355	169	186
Total	385	175	210

symptoms, when they were present, is shown in table III Only breathlessness seemed to have any relation to the level of the hæmoglobin, being complained of more frequently as the anæmia was more severe (fig 1 and table IV) The other symptoms were not significantly increased as the level of the hæmoglobin fell

As it is generally held that many normal pregnant women complain of breathlessness, the diagnostic significance of dyspnœa is greatly reduced However, of a consecutive series of 100 " normal " pregnant women, at or before six months' pregnancy, with a hæmoglobin level above 10 g there was breathlessness in only 17%, compared with 45% in the anæmic group (fig 1 and table III) As almost all the anæmic women were interviewed before six months' gestation their dyspnœa is unlikely to have had a mechanical origin

Clinical Signs

As is well known, it is quite unsafe to diagnose anæmia on clinical evidence alone This is amply proved in this investigation Nearly half the cases (385) with hæmoglobin below 9 5 g had no clinical signs of anæmia Of 385 cases 210 (54 5%) had clinical evidence of anæmia—i e, obvious pallor of the skin or conjunctivæ, or both The relation of these appearances to the level of hæmoglobin is seen in table V, which shows that, when hæmoglobin is between 7 0 g and 9 5 g, half the cases show signs of anæmia, and that when it is between 6 0 g and 6 9 g three quarters of the cases do so It is only when the hæmoglobin is below 5 9 g that all the patients are clinically anæmic In other words, it is quite impossible to be sure of excluding anæmia clinically when the hæmoglobin is between 6 0 g and 9 5 g, and the great bulk of anæmia in pregnancy lies in this group

TABLE VI—PREDISPOSING FACTORS IN HISTORY

Total 400 cases

Blood loss	
Menorrhagia	97 (*24*%)
Bleeding piles	35 (*9*%)
Epistaxis	25 (*6*%)
Previous anæmia in pregnancy	100 (*25*%)
Pulmonary tuberculosis	11 (*2 5*%)
Diet	
Never ate meat	26 (*6 5*%)
Seldom ate meat	177 (*44 2*%)
Never ate vegetables	11 (*2 5*%)
Seldom ate vegetables	48 (*12*%)

Berry and Cowin (1950) found in school children that the colour of the gums was unreliable as an index of hæmoglobin level

Silverman (1954) observes the colour of the palmar creases in judging the severity of the pallor He notes that when the red colour of the creases is lost, the hæmoglobin may be judged as being below 7 0 g However, this is a severe degree of anæmia, and such a sign cannot be depended on in diagnosing milder grades of anæmia

Hæmoglobinometry is essential in diagnosis as well as in assessing progress It should certainly be routine at the first antenatal visit and again a few weeks before term Abnormal changes were found in the nails of 43 women (11 2%) 14 of these had koilonychia, 12 flat nails, and 17 friable or breaking nails These nail changes were seen mainly in chronic cases At least a third gave a history of having been treated for anæmia previously The [illegible]age parity in this group was 5 7, against the average 3 8 for the total attendance at the Hospital in 1953 The hæmoglobin was often very and averaged 7 g in the 43 cases

Ætiology

The history of each patient included questions possible factors in the production of anæmia Table shows the results, and from these findings it can be concluded that blood loss and intercurrent disease are not primary causes, occurring in not more than a third of the cases (antepartum hæmorrhage was excluded from the series)

The average parity of the total attendance at the Rotunda Hospital during 1953 was 3 8 In 384 severe anæmias the average parity was 4 8 This indicates that parity may be a factor, and in fact the incidence of severe anæmia was found to increase with parity, though not so much as one might expect (fig 2) Doyle and McGrath (1954), dealing with the same population, which there is often a high parity, came to the sa conclusion, but other workers, notably Bethell et (1939), Scott and Govan (1949), and Lund (1951), ha not found this relation

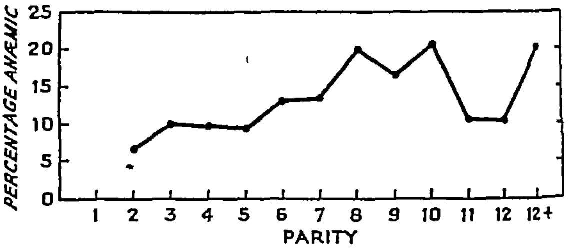

Fig 2—Relation of parity to anæmia.

The only remaining possible factor is inadequa supply of elements essential for formation of hæmoglob As absorption and utilisation are rarely at fault, defective diet is almost certainly responsible From brief questioning of these patients, the most strik finding was the lack of meat in their diet Half of th either never or very seldom ate meat Most of them vegetables besides potatoes indeed only 14% s they seldom or never ate vegetables Protein deficien may be a factor, but there is no doubt that almost these cases respond very well to iron As the main sour of iron are green leafy vegetables, which become sca in late winter and in spring in Dublin, one would exp iron deficiency to increase at this time This is bor out by our figures (see above), and our finding agr with those of Scott and Govan in Glasgow and Do and McGrath (1954) in Dublin This seasonal variati may also be due to the diet containing less vitamin at this time Lund and Kimble (1943) have ascribed similar seasonal incidence to lack of vitamin C T patients were not specifically questioned about oth important iron-containing foods, such as oatmeal a liver

Iron Therapy

At the beginning of the investigation all the wome with anæmia were given a supply of gr 3 ferrous sulphat

TABLE VII—TOLERANCE TO DIFFERENT IRON COMPOUNDS

—	Ferrous sulphate	Molybdenised ferrous sulphate	Ferrous gluconate
Able to tolerate	92 (*46*%)	50 (*55*%)	93 (*84*%)
Unable to tolerate	97 (*48*%)	38 (*41*%)	9 (*8 1*%)
Tolerated with difficulty	18 (*9*%)	3 (*3 3*%)	7 (*6 3*%)
Total	207	91	109

TABLE VIII—COMPARISON OF RESPONSES TO FERROUS SULPHATE AND FERROUS GLUCONATE

(Initial values were at 6 months gestation)

—	No of cases	Initial Hb (g per 100 ml.)	Range of increase in 3 mos (g per 100 ml)	Average increase in 3 mos. (g per 100 ml.)
Ferrous sulphate	13	8·0–8·9	1·6–4·0	2·4
Ferrous gluconate	13	8·0–8·9	1·8–3·9	2·6

tablets † and instructed to take two tablets thrice daily It was soon found that many women complained that they could not continue to take them usually owing to nausea or vomiting These women were then given either 'molybdenised' ferrous sulphate ‡ or ferrous gluconate § in the same dosage (six tablets daily) 91 women were given molybdenised ferrous sulphate, and 100 ferrous gluconate from the start of treatment The rate of tolerance for these three compounds is shown in table VII About half the women could not tolerate ferrous sulphate and 41% could not tolerate molybdenised ferrous sulphate but only 8% were intolerant of ferrous gluconate.

The hæmatological responses to each of these hæmatinics were compared. To eliminate error only cases conforming to the following criteria were selected (1) the hæmoglobin had been estimated monthly from the sixth to the ninth month of gestation (2) six tablets had been taken daily with absence of intolerance and (3) the initial hæmoglobin values had been comparable (8·0–8·9 g per 100 ml) Of the 307 anæmic women 31 fulfilled these criteria 13 had been treated with ferrous sulphate and 13 with ferrous gluconate, and there was little difference in response (table VIII) It has been stated previously that ferrous gluconate gives a better response than does ferrous sulphate (Haler 1952 Lillie et al 1954) but on further analysis little difference is evident Previously reported differences are probably due to differences in toleration The women treated with molybdenised ferrous sulphate are too few for comparison, but the average response of 5 of them under the same criteria, was +2·2 g per 100 ml , which was not significantly more than the response to ferrous sulphate Other workers (Dieckmann et al 1950, Benstead and Theobald 1952) have reported a better response with this preparation

Saccharated oxide of iron || was used intravenously whenever oral iron was not tolerated when there was no response to oral iron or when anæmia was discovered first in the last few weeks of pregnancy Very few cases did not respond to one or other form of iron therapy and these were all found to be cases of megaloblastic anæmia of pregnancy (Moore et al 1955) The usual course of intravenous iron was an initial dose of 50 mg followed by 100 mg daily for the first week and thence forward on alternate days for not more than three weeks In all cases of iron deficiency the response was rapid About 20 cases were treated in this way in the year (5% of the severe anæmias), and the average increase in hæmoglobin was 2·4 g per 100 ml in two or three weeks

Discussion

This common anæmia in pregnancy is attributed to inadequate diet and our findings support this explanation though in a negative way Doyle and McGrath (1954) who studied the same population show conclusively a relation between defective diet and anæmia and it has long been established that a diet poor in protein and iron is the cause of pregnancy anæmia (Strauss and Castle 1932, Bethell et al 1939, Edwards et al. 1953) In fact the incidence of anæmia in pregnancy is a fairly reliable index of the standard of diet of the mothers.

If iron deficiency is slight the hæmoglobin though it decreases may remain above 10 g per 100 ml and be considered 'physiological' Davis and Jennison (1954) point out that even women with initial hæmoglobin levels of 10–13 g benefit from iron therapy We noted that with iron treatment the hæmoglobin rose in many cases to 12–14 g well above the usual levels of the 'physiological anæmia' of pregnancy Benstead and Theobald (1952), Fisher and Biggs (1953) and Davis and Jennison (1954) have all drawn attention to this increase in hæmoglobin to normal (non pregnant) levels in late pregnancy with efficient iron therapy

It has been argued that a mild degree of iron deficiency is of little importance and that in most cases women with it have successful pregnancies without trouble. On the other hand it is obviously desirable that a woman should reach term with her full complement of hæmoglobin and therefore be in a good state to withstand any abnormal blood loss. It seems reasonable and good practice to give an efficient preparation of iron to every pregnant woman during the last trimester to counteract iron deficiency

Summary

On first attendance at the antenatal department, Rotunda Hospital, Dublin, 1 out of every 4 women is anæmic

The incidence of anæmia rises in the winter

Breathlessness is the commonest symptom and appears to be related to the degree of anæmia, but many cases are without symptoms

It is impossible to be sure of recognising anæmia by clinical means unless the hæmoglobin is below 6 g per 100 ml Hæmoglobinometry is essential Spoon shaped or breaking nails indicate long-standing anæmia.

A diet deficient in iron is the most important cause of this anæmia A case is put forward for the routine administration of an efficient iron preparation in every pregnancy

Ferrous gluconate was tolerated well in 90% of cases, whereas ferrous sulphate (whether molybdenised or not) was tolerated in only 50%

In the absence of intolerance, there is little difference in the hæmatological response to ferrous sulphate and ferrous gluconate

We are grateful to the master of the Rotunda Hospital (Dr E W L. Thompson) whose coöperation made the investigation possible and to the director of pathology (Dr H C Moore) for his helpful criticism and his unfailing interest and assistance A grant to one of us (E. W L.) from the Medical Research Council of Ireland is gratefully acknowledged Messrs. Evans Medical Supplies provided the ferrous gluconate

REFERENCES

Benstead, N Theobald G W (1952) *Brit med J* i, 407
Berry W T C, Cowin P J (1950) *Brit J Nutr* 4, 1
Bethell F H Gardiner S H MacKinnon, F (1939) *Ann intern Med* 13 91
Davis L R, Jennison R. F (1954) *J Obstet Gynæc., Brit Emp* 61 103
Dieckmann W J (1945) *J Amer med Ass* 128 485
— Priddle H D., King J A Forman J B (1950) *Amer J. Obstet Gynec* 59 442.
— Wegner, C R (1934) *Arch intern. Med.* 53 71 188 345
Doyle G D , M Grath, J (1954) *Irish J med Sci* p 414
Edwards C H Mitchell J R., McHarge F J., Trigg L., Jones L. (1953) *J nat med Ass., Tuskegee Ala* 45 150
Fisher M Biggs R (1953) *Brit med J* i 402.
Haler D (1952) *Ibid* ii 1241
Lillie E. W Gatenby P B B., Moore H C (1954) *Irish J med Sci* p 304
Lund C J (1951) *Amer J Obstet Gynec.* 62 947
— Kimble M S (1943) *Ibid* 46 635
Moore H C, Lillie E W Gatenby P B B. (1955) *Irish J med. Sci* p. 106
Scott J M., Govan, A D T (1940) *Brit med J* ii 1083
Silverman, J J (1954) *J Amer med Ass* 155 902
Strauss M B Castle W B (1932) *Amer J med. Sci* 184 663

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† Feroxan tablets (ferr sulph. exsicc. *B.P.* gr 3 cupr sulph *B.P.* gr $^1/_{64}$ mang sulph *B.P.C.* gr $^1/_{64}$)
‡ Mol Ironia tablets (ferr sulph. exsicc 195 mg ; moybdenum sesquioxide 3 mg)
§ Ferlucon tablets (ferrous gluconate 300 mg ; aneurine hydrochloride 1 mg)
|| Ferrivenin

TREATMENT OF MENTAL DISEASE BY SLEEP

O V Kerbikov

DIRECTOR OF THE PSYCHIATRIC CLINIC OF THE 2ND MOSCOW MEDICAL INSTITUTE

In recent years sleep therapy has been studied increasingly both by clinicians and by research workers Complete monographs (Baumann 1953, Angel 1953), and even special issues of journals, have been devoted to the subject But, though its value in certain disorders has been established, many theoretical aspects need further investigation, and much has still to be done to improve the results

Historical

The method has a long history Pierre Janet points out that the treatment of psychoses by prolonged sleep was practised in the early part of last century, when "animal magnetism" was in vogue At the end of that century there was in Sweden a hospital (Janet calls it the Palace of the Sleeping Beauty) where prolonged sleep was the basis of all treatment For mental illness rest in bed was introduced by Korsakov about that time, and came to be widely practised in Russian mental hospitals

Pavlov's work on cortical inhibition and its protective and therapeutic nature supplied the scientific explanation of the method Pavlov showed that inhibition was a protective physiological function developed by the nerve-cell in the course of phylogenesis His work led clinicians to reject deep narcosis in favour of intermittent deep sleep lasting 10–20 hours daily, and to formulate indications for treatment

The main indication for sleep therapy is in patients developing protective inhibition Sleep therapy is less valuable in excited patients than in those showing depressive inhibitory states Treatment based on these principles was introduced in Ivanov-Smolensky's and Protopopov's clinics in 1943–46, and the same principles guide therapeutic practice in Soviet hospitals and clinics today

Nevertheless, the simple formulation of the basic indications leaves many practical problems unsolved, since protective inhibition is seen in a variety of symptoms and syndromes, not all of which respond effectively to sleep therapy Moreover, patients react very differently to any given narcotic Baumann (1953) and others have shown that for patients with an excitable nervous system barbiturates seem most effective, whereas those in whom inhibition predominates respond best to chloral hydrate Hence a wide range of soporific agents is needed

So that we can use smaller doses of drugs, everything is arranged in the sleep-therapy wards to facilitate sleep The action of the drugs is reinforced by monotonous stimuli—e g, the sound of a muffled metronome or the flashing of a blue light—and by heat in the form of hot-water bottles or ozocerite poultices Various methods of conditioned sleep are also employed

Electro-sleep

In our investigations, attention focused first on "electro sleep," developed in 1946 by Gilyarovsky et al The results in 80 patients were discussed by my colleague Korkina (Electro sleep should not be confused with electro-narcosis, which we abandoned because of the serious risk of convulsions, opisthotonos, and subcomatose states) Electro sleep uses a weak electric current, applied as a rhythmic stimulus A direct current is used, with square waves, an impulse duration of 0 2–0 3 milliseconds, and a frequency that can be regulated [illegible] per second The amplitude of the current varies from 5 to 15 mA. Electrodes are usually applied in orbito occipital position

When the current is switched on, a slight pulsa felt deep behind the eyes and a slight pricking in eyelids (I have checked this many times on my After 15 or 30 minutes most patients begin to feel sl and gradually they fall asleep The sleep is often ac panied by dreams, and it may persist after the is switched off Some patients, on the other hand, nev experience more than a feeling of drowsiness

A course of treatment consists in ten to twenty da applications, each lasting 2 hours In severe insom the application is sometimes extended to 4 hours a d With children the length of treatments is reduc to 40 minutes, and the amplitude does not exce 5–6 mA.

Electro sleep produces no clinical evidence of vegetat or somatic disturbance, and is apparently innocuous expe ments on animals have revealed no somatic contra indicatio We deem it prudent, however, not to use electro sleep i patients with severe myopia, glaucoma, or gross cardi insufficiency

An electro encephalogram taken immediately after a trea ment shows a general reduction of cortical electro-activit In some patients normal electrical activity was restored t the cortex after a period of heightened activity This may b a peculiarity of electro sleep, since reduced activity is usu after narcotic sleep Investigations of neurodynamics b Ivanov Smolensky's method (Kirilova) showed that electr therapy often abolishes disturbances in differentiation phasic phenomena disappear, and the tendency for con ditioned motor reactions to become readily exhausted corrected

Results

The best results have been obtained with neuroses an psychogenic reactions displaying asthenia and asthen depression but without severe psychotic featur Permanent benefit was not obtained in obsessional state Presenile psychoses with anxiety or agitated depressio often become worse, and in such states electrotherapy contra-indicated With schizophrenia, there is an improve ment in the early neurotic-like phases, and in the reactiv forms

Among the advantages of electro sleep are the almo complete absence of somatic contra-indications and th possibility of its use in outpatients Drawbacks includ the difficulty of regulating the depth and length of slee the fact that some patients do not sleep during the treat ment, and the impossibility (for technical reason of applying it to disturbed patients, to patients wit delusions of physical influences, and to patients showin negativism

Mechanism

The mechanism of electro sleep has not been full explained Gilyarovsky et al (1952), as well as Serv (1954), who introduced the method in Czechoslovak emphasise the direct effect of the electric impuls on the brain Other investigators deny the pos bility of direct influence on the brain of such current and suggest that the effect is produced by wea rhythmical stimulation of the peripheral receptor Observations at our clinic show that sleep can often b produced by the application of the electrodes to th forearms, without direct application of the current o the brain Yet the fact that presenile patients get wors with this method suggests a central action of the curren since it is difficult to suppose that weak stimulation of the peripheral receptors could have th effect

Alcohol-induced sleep

Since 1949 we have in our clinic induced prolon sleep by intravenous infusion of an alcoholic sol The results in 150 patients were summed up by Ilyinsk

Though alcohol has been used by many workers for the disinhibition, temporarily, of stuporose patients (Ivanov-Smolensky 1952, Gilyarovsky et al 1952) it has not, so far as we know, been used routinely in sleep treatment. The following considerations led us to turn to ethyl alcohol as a sleep-producing medium in the treatment of mental disease, especially schizophrenia.

(1) Well-developed schizophrenia and alcoholism are seldom found together.

(2) Alcohol is an "endogenous" narcotic in that it is a normal product of metabolism.

(3) The combustion of alcohol conserves other calorigenic substances, proteins in particular. It assists in the oxidation of glucose and in its utilisation by the tissues (Meyer 1935 and others).

(4) Alcohol is a component of many blood-replacement fluids and medicines used to combat shock.

After studying the short-term and long-term effects of alcohol in dogs and demonstrating the harmlessness of appropriate doses of the alcoholic mixture on ourselves we proceeded to treat patients with intravenous infusions of the following mixture:

Pure alcohol 96%	60 to 120 g
Sodium chloride	4 g
Calcium chloride	1 g
Glucose	25 g
Distilled water	to 500 ml.

500 ml. of this mixture is given over a period of $1^1/_2$–2 hours. Daily infusions are made, with intervals of 1–2 days after each period of 4–6 days. A course of treatment comprises twelve to fifteen infusions.

Two phases are usually noted in the condition of the patient during each infusion: (1) the phase of disinhibition, which comes on after the administration of 200–350 ml.; and (2) the phase of sleep, which comes on after 250–450 ml. In the first phase there is a combination of euphoria and sleepiness. In the second, the depth of sleep depends on the speed of the infusion. In some patients, and also if the infusion is given rapidly, the first phase is absent. The duration of sleep after each infusion is about 3–5 hours. In patients who formerly abused alcohol sleep may be delayed until as long as 40 minutes after the infusion is completed. Rarely it does not come on at all.

Results

Investigation showed that for 3–5 hours' sleep a blood-alcohol level of 100–170 mg. per 100 ml. was needed, which means that 1·2–1·8 g. alcohol per kg. body-weight must be introduced. During the injection there is flushing of the face and the upper part of the chest, moderate sweating, and diuresis. The blood-pressure falls by 10–20 mm. Hg but returns to its previous level 2–3 hours after the end of the infusion. The patient's appetite is usually increased, refusal of food ceases, and they gain weight; hence we use this method—but with a reduced dose—in weak exhausted patients, and in those who refuse food; and no other method gives such good results.

Among schizophrenics, good remissions were obtained in about half the cases. The best results were in patients with protective inhibition. Good results were obtained in 80% of a group of patients with psychogenic reactive states, mostly of a pronounced psychotic nature, and these patients were enabled to resume their former work. Less satisfactory results were obtained in patients in this group who had an environmentally conditioned hysterical reaction of primitive type. We do not, of course, treat children by this method.

There have been few complications: mild phlebitis has occasionally developed, and some patients have vomited after high doses of the alcohol. In some 2000 infusions we have never had occasion to use cardiac or respiratory stimulants. The commonest technical difficulty is to find suitable veins.

Amylobarbitone and Caffeine

In the past few years my colleague Yagodka has developed a method of using amylobarbitone ('Amytal') and caffeine—drugs which are usually regarded as of value only in the diagnosis of inhibitory states. We have used caffeine (0·2 g. intramuscularly) and soluble amylobarbitone (3–10 ml. of a 5% solution intravenously) routinely, in courses of 10 to 60 daily injections. A few minutes after the short-lived disinhibition and euphoria have passed, many patients doze off during the day and sleep significantly better at night.

This method does not seem to have a very wide scope in schizophrenia; but our results in 70 patients with neuroses, asthenia, and chronic reactive states were good. Obsessional states resistant to all other forms of treatment sometimes yielded to this method. Even temporary relief from painful experiences, by gradually abolishing the pathological conditioned reflexes, seems to hasten recovery.

Nitrous Oxide

Though the euphoric and narcotic properties of nitrous oxide were discovered more than 150 years ago, so far as we know no consistent efforts have been made elsewhere to use 'laughing gas' in psychiatric practice. Our colleagues Zharikov and Matveyev have used it routinely in the treatment of depressive and agitated patients and those suffering from insomnia. As technical difficulties made it impossible to carry out a long course of treatment by inhalation of nitrous oxide, the gas was introduced subcutaneously, where it provided a depot that was later absorbed slowly into the tissues. Experiments on cats showed that 400 ml. of gas injected under the skin was absorbed by the end of 24 hours. Zharikov and Matveyev carried out many similar experiments on themselves.

Each injection is followed by a feeling of lightness and euphoria, and eventually by sleepiness which lasts 4–6 hours. The following night sleep is deeper and longer than usual. When 300–500 ml. of gas is introduced under the skin there is a sensation of bubbles running in different directions, but crepitation disappears completely within 24 hours.

32 cases of mild reactive depression, involutional depression, and cyclothymia were treated, each receiving some 400–500 ml. of gas at each of 12 injections. It is too early to assess the results, but it is clear that sleep is improved. The patients often sleep for 2–3 hours after the injection, and many need less sedation at night. Most are improved in mood and experience a sense of well-being. Whether these effects are lasting cannot yet be stated.

BIBLIOGRAPHY

Angel J M. (Cited in *La Raison* 1953 no. 6)

Baumann R. (1953) Physiologie des Schlafes und Klinik der Schlaftherapie. Berlin.

Delay J., Mallet, J (1948) *Encéphale* 37 99

— — Roubleff I (1948) *Ibid* p 57

Fogel E J Gray L P (1940) *Amer J Psychiat* 97 677

Gilyarovsky V A., Liventsev A. M., Segal Y E *Kirilova Z. A (1952)* Electroson.

Ivanov-Smolensky A G (1952) Ocherki patofiziologii vysshey nervnoy deyatelnosti.

Janet P (Cited in *La Raison* 1953 no 6)

Kameneva E N Yagodka P K. *(1945–46) Amer Rev Sov Med.* 3 348

Kanal, I (1933) *Biochem. Z* 262 41

Kerbikov O V., Zorina, E. S (1950) *Zh. Nevropat. Psikhiat* 6, 43

Lechenie Snom Trudi zasedaniya prezidiuma Akademii meditsinskikh nauk S.S.S R. Feb. 27–28, 1953

Meyer M. H (1935) *Biochem. Z* 276 174

Pavlov, I P Polnoe Sobranie Trudov (1949) *Izd. Akademii Nauk. S.S.S.R.*

Protopopov V P Patofiziologicheskie Osnovi Rationalnoy Terapii shizofrenii. Kiev 1946.

Servit, Z (Quoted in *Zh. Nevropat. Psikhiat. im. SS Korsakova* 1951 5 415).

Starkov P M. (1950) *Gazovy Narkoz.*

INTRA-ARTERIAL TRANSFUSION BY THE FEMORAL ROUTE

RICHARD NEVE *
M B Lond , F R C S
LATE SENIOR SURGICAL REGISTRAR, SOUTHMEAD HOSPITAL, BRISTOL LATE REGISTRAR, PROFESSORIAL SURGICAL UNIT, UNIVERSITY OF BRISTOL

As a means of combating arterial hypotension, intra-arterial blood-transfusion has been used for more than ten years This method is needed but occasionally in cases of extreme emergency, and the femoral route offers many advantages, both in the ease of giving the transfusion and in the freedom from risk

An apparatus simple to maintain and easy to use is essential That described here fulfils most of the criteria of simplicity and safety It can be constructed from standard blood transfusion equipment with a few additions, and a stand for it is within the capabilities of most hospital workshops for the cost of a few pounds

THE APPARATUS (fig 1)

Positive pressure is provided by an aneroid sphygmomanometer Between the inflated arm band (which acts as an air reservoir to maintain constant rather than intermittent pressure) and the pressure gauge is inserted a T piece which is connected to the air intake on the bottle The bottle is held in a quick release clamp in the stand so that no screw top need be used to prevent leakage The efferent tubing is led through a Macintosh valve, and a spring clip on a 1 in. length of rubber tubing is used to control its sidepiece The tubing then passes to a ' Record ' fitting, such as is used on standard blood giving sets for connection to the needle A Greenfield's lumbar puncture needle has been found to be the most satisfactory The stilette is modified so as to project for $^1/_2$ cm beyond the end of the needle point and is rounded (fig 2) Two artery clips are convenient for controlling the flow whilst filling—one above and one below the valve

A two way apparatus (fig 3) has also been designed. This simplifies the giving of more than one bottle at a session by changing the positions of the clips The second bottle can be given while the first is changed, and so forth

Preparation for Use

The transfusion tubing, carrying valve and needle, are sterilised and kept in a drum. When the apparatus is the proximal end of the tubing carrying the filter is in into the bottle This slides into the screw clamp Precaut must be taken to ensure that the ground glass plunger in Macintosh valve is freely movable before blood is to fill it Air is excluded in the normal way and the dis end of the transfusion tubing is plugged into the sidep of the Greenfield's needle The main channel of the need houses the stilette which must be withdrawn before punc the vessel, and it is not until the needle is well within the artery that the position of the tap is changed so as to perm blood to enter the needle from the tubing

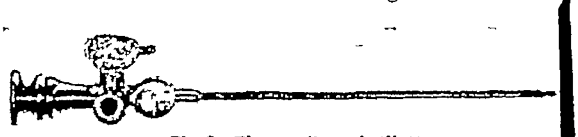

Fig 2—The needle and stilette.

TECHNIQUE OF ARTERY PUNCTURE

The femoral artery can usually be punctured percutaneous and it may be made more prominent by external rotati and extension of the leg over a sandbag under the buttock The needle should enter immediately below the inguin ligament in an upward direction, since the femoral vess rapidly recede beneath the adductors as they leave the femo triangle and become *relatively less accessible* If any difficult is experienced in locating the artery or puncturing it, there should be no hesitation in cutting down and exposing through a vertical incision downwards from the inguinal ligament at its mid point

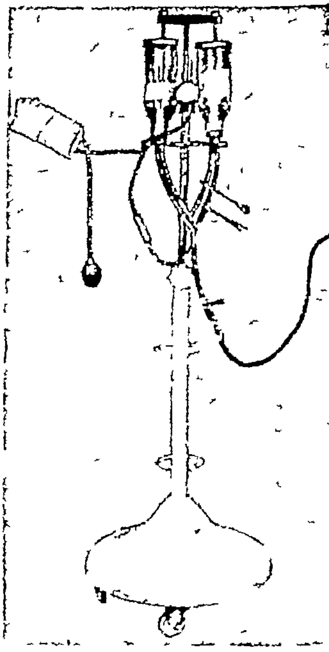

Fig 3—The double apparatus.

The Greenfield's needle has been adopted since it has a wide enough bore to provide for rapid transfusion and is long enough to allow the operator to steady it easily whilst leaving $1^1/_2$–2 in within the lumen of the artery It has a short bevel and is unlikely to damage the opposite wall of the vessel as it enters The stilette is removed and as the needle point enters the artery, arterial blood will spurt back. The stilette is immediately reinserted and with its round end projecting, the needle is advanced towards the umbilicus for 1 to 2 in It is now firmly gripped by the vessel and need *not* be *held* When it has been advanced to the desired point, the stilette is withdrawn the tap turned through 90°, cutting off the open end of the needle and connecting it to the transfusion tubing

The screw clamp on the stand absolutely prevents an leakage around the bung It has not been found nec to use locking connections on the rubber tubing or to them, since if rubber and glass connections are chosen fully they withstand pressure well up to the range required and when the rubber perishes and starts to stretch it shou be renewed

A Macintosh valve renders air embolism almost impossib but a manually operated source of positive pressure has selected since the need to maintain the pressure by hand w necessitate the constant presence of the operator

ADVANTAGES OF THE METHOD

The femoral artery is the best site for intra arter transfusion for two reasons First, the vessel is

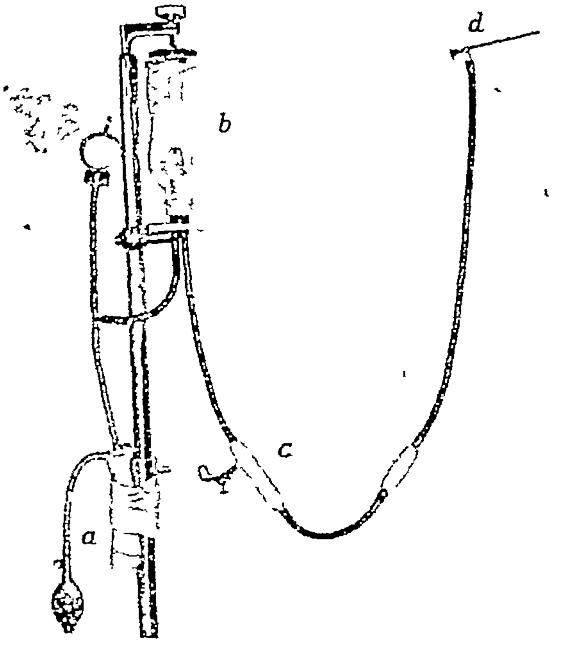

Fig 1—The single apparatus: (a) aneroid sphygmomanometer (b) bottle in quick release clamp , (c) Macintosh valve , (d) Greenfield's needle

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* Now at Kimberley, British Columbia Canada

nctured percutaneously in many cases and even if
tting down is involved, this is a simpler and quicker ethod than cannulating a radial artery which may be severe spasm (Porter et al 1948) and less shocking than tering the position of the patient to allow transfusion the lumbar route (Haxton 1953)

Secondly, the method is freer from complications— any rate than the radial route

Gangrene of finger tips, and in one case of the thumb s been reported after using the radial artery In two cases orter et al. 1948 Seeley 1949) the use of dextran or plasma s been incriminated as the cause and the gangrene appears have been the result of perfusing a peripheral artery with noxygenated fluid. One would expect there to be less danger this when a large vessel such as the femoral is used and hen there is adequate opportunity for the transfused fluid mingle with oxygenated blood before being carried to the tremity of the limb

In a further case (Bingham 1932) gangrene of the digit llowed the use of blood presumably owing to an anatomical nomaly—a further risk to radial-artery ligation

Thrombosis of the femoral artery following intra arterial ansfusion has occurred in one case (Liaras et al 1949) n this, the thrombosis was at the site of needle puncture l cm below the inguinal ligament) in a patient of 72 after 50 ml of plasma had been given The proximal site of thrombosis seems to exclude the plasma as the cause and the mb recovered after embolectomy A massive extravasation f blood was found at the site of thrombosis which points ither to leakage around a needle which was only just in the rtery or to damage to an atheromatous plaque The former isk can be obviated by the technique I have described he latter is intrinsic in the use of artery puncture in n atheromatous vessel. It has seldom occurred following he wide use of the femoral artery for arteriography

Vascular spasm often follows puncture of the femoral rtery but it can be expected to resolve spontaneously Relief of spasm can be rapidly obtained by the direct pplication of papaverine (Kinmonth 1952) if the vessel as been exposed

I am indebted to Prof R. Milnes Walker Mr W M Capper Mr J A. Pocock, on whose patients intra-arterial trans ons have been performed to Mr R. E Horton for help l encouragement in the preparation of this paper; to A. E Christmas F.I.B.S.T., who helped to design the ck release clamp and built the single headed apparatus l to the group engineer's department at Southmead spital who built the double apparatus.

REFERENCES

gham D L. C (1932) *Lancet* ii 157
xton, H A (1953) *Ibid* i 672
nmonth, J B (1952) *Brit med J* i 59
ras Xicluna, and Leca (1949) *Afr franç chir* p 237
ter M. R., Sanders E K. Lockwood, J S (1948) *Ann Surg* 128, 865
ley S F (1949) *Amer J Surg* 78 733

DOES REDUCED BLOOD-SUPPLY CAUSE PAIN?

MICHAEL KELLY
M.D Adelaide

STANHILL MEDICAL CENTRE, MELBOURNE AUSTRALIA

DURING the past twenty years ischæmia has become a andard explanation for pain of unknown origin

Stitch is said to be due to ischæmia of the diaphragm apps 1941) trigeminal neuralgia to paroxysmal ischæmia deep facial structures (Karl et al 1945); headaches to lative ischæmia of cranial muscles (Tunis and Wolff 1954) on articular rheumatism (Ray 1934) decompression pain ahlstrom et al. 1930) proctalgia fugax (Ryle 1942) smenorrhœa (Woodbury et al 1947) and many other pains ve been attributed to ischæmia.

But apart from coronary insufficiency, intermittent laudication arterial embolism and arterial spasm w pains are certainly attributable to reduced blood upply In most cases we have no evidence of ischæmia nd are guided chiefly by analogy—especially by the classical experiments on constriction pain in working muscle (MacWilliam and Webster 1923 Lewis 1932, 1942)

The fist is repeatedly clenched while the circulation of the arm is arrested with a manometer cuff There is no pain if the muscles are not worked but the forearm muscles become painful and tender after 20 contractions—intolerably so after 40 When the cuff is released the pain vanishes in 3 seconds

Factor P is not Produced by Anoxia

Lewis believed that a chemical substance (factor P) was produced by working muscles without oxygen and diffused out to the pain nerves in the tissue spaces But the forearm is not ischæmic it is congested with venous blood Moreover, there is ample proof that the pain is not due to lack of oxygen

(1) The pain comes after 20 contractions whether the forearm is congested by a manometer cuff or exsanguinated by an Esmarch bandage (my observations)

(2) The pain comes after 35 contractions when the manometer pressure is at 50 mm Hg—the circulation is not occluded (my observations)

(3) The pain appears after 60–100 contractions in a forearm exsanguinated by digital pressure on the brachial artery alone—not on muscles or nerves (Kelly 1955)

(4) Anoxia which causes dyspnœa and cyanosis does not accelerate the onset of pain (Harpuder and Stein 1943)

(5) The onset of pain is not accelerated by vasoconstriction or delayed by vasodilatation (Rein and Schneider 1937 Lewis et al 1931 Harpuder and Stein 1943)

(6) Resting muscles, and even non muscular tissues, generate pain when the constricted limb is put in hot water for 5 minutes (Harpuder and Stein 1943) After a shorter heat stimulus 8 to 12 contractions will generate pain

Factor P is not a Circulating Biochemical Substance

Though factor P does not appear during 30 minutes circulatory arrest it remains stable (said Lewis) once it appears Yet the pain vanishes as soon as the circulation is restored Factor P is not a known metabolic product the pain is not influenced by changes in the pH (Matson and Forster 1936) or by lactic acid or histamine (Harpuder and Stein 1943) Factor P cannot be detected in the circulating blood Harpuder and Stein generated ischæmic pain in both legs and tried to flood the system by releasing both femoral cuffs at once Then the usual 20 contractions were required to generate pain in the forearm

Can a stable chemical product become unstable when the blood flows? This would require its destruction by an anti factor which had disappeared from the forearm yet is normally in excess in the blood. Such a potent substance would surely have been discovered ere this. The only other possibility (if factor P is a chemical substance) is that it is washed away—i e it must be diffusible The chlorides of sodium and potassium are diffusible and we know something about muscle pains which they cause

(1) 1% potassium chloride solution injected into the nutrient artery to a muscle causes severe pain for 45 minutes (Harpuder and Stein 1943)

(2) Hypertonic saline solution injected intramuscularly causes pain for more than 30 seconds (Lewis 1942)

Therefore the pain from an undetectable circulating substance would not be likely to disappear in 3 seconds

Factor P and Muscular Fatigue

Whenever I have made the experiment I have noticed a feeling of fatigue and muscular weakness increasing to paralysis The increasing tightness of the cuff gradually merged with the fatigue into intolerable pain I was once dissecting in tight rubber gloves when the fingers became weak and almost paralysed fatigue appeared in the forearms and progressed until it was exactly like ischæmic pain

The muscles take 20 minutes to recover If they are worked again in 10 minutes the pain comes after 12 contractions, and if they are fatigued from normal work, less than 20 contractions are required (Lewis 1942) Fatigue can do what neither vasoconstriction nor anoxia can do—intensify ischæmic pain Fatigue is not only an inability to contract, it is also a muscular sensation which intensifies to pain and tenderness

Partial Nerve block

When the vessels are occluded, cutaneous sensory disturbances are produced by pressure on nerves (Lewis et al 1931, Barlow and Pochin 1948, Sinclair 1948, Merrington and Nathan 1949, Addis et al 1950) The forearm goes numb when the cuff has been inflated for 10 minutes, and for shorter periods after nerve injuries (Gilliatt and Wilson 1953, Marshall et al 1954) Perhaps the pain and tenderness are also neural, it is well known that muscles recovering from nerve injury are liable to fatigue and painful cramps

When I partially blocked my ulnar nerve with procaine at the medial epicondyle, I felt aching pain in the hand and the ulnar side of the forearm after 30 clenchings of the fist When my lateral popliteal nerve was compressed, and the ankle was rapidly flexed and extended, pain and tenderness developed in the anterior muscles but not in the calf (Kelly 1955) If the pressure was released while the movement went on, the pain vanished

While the limb is constricted, there is an intensified electric discharge from the compressed nerve and its peripheral field (Kugelberg 1946) Muscular coördination is poor, and deep reflexes are absent (Gellhorn and Thompson 1944), muscles become weaker after 20 minutes even if they are not worked (Marshall et al 1954) Painless lesions of skin (blister) and muscle (saline solution injected) become painful and generate more impulses (Nathan 1953) When he compressed the nerve alone Nathan generated muscular and cutaneous pain as before, though the circulation was free

Heat, Hyperalgesia, and Factor P

The constricted limb becomes generally hypersensitive, skin hyperalgesic (Sinclair 1948), and deep wounds painful (Addis et al 1950) Heat not only intensifies factor P in muscles, but also causes burning pain in a constricted finger (Harpuder and Stein 1943) Lewis (1942) showed that heat intensified erythralgic cutaneous hyperalgesia to burning pain, the constricted finger and the ischæmic muscle are therefore hyperalgesic

An artificial lesion in muscle becomes spontaneously painful (by summation) when its nerve is compressed (Nathan 1953) If a fatigued muscle is substituted for a tender spot, again the threshold is lowered by compression of the nerve Muscular fatigue is therefore a hyperalgesic state which is intensified to pain by partial nerve-block

Ischæmia is not a Common Cause of Pain

The causation of pain is usually multiple (Wikler 1953) Several subthreshold factors combine to give threshold stimulation Often the cause which seems most likely is merely one of the effects of a deeper common cause Cardiac pain is often due to reduced coronary circulation, but additional factors are required to precipitate the pain, which is absent for long periods in every case Pain from arterial embolism (Lewis 1936) and intermittent claudication (Boyd et al 1949) usually depends on factors additional to loss of blood-supply In Raynaud's phenomenon lesions of nerves are partially responsible (Marshall et al 1954) Causalgia after nerve injuries is not more common when the main artery has been severed (Sunderland and Kelly 1948)

When we say that a common but obscure pain (the stitch) is due to ischæmia of muscle, we are guided by [illegible] and not by observation Deep and widespread [illegible] re often associated with tenderness of muscles Sometimes a primary muscular lesion is res for radiating pain and tenderness (Kellgren 1 Sometimes, on the other hand, the muscular pain tenderness are reflex—secondary to visceral or deep lesions (Sinclair et al 1948) Because we that ischæmia causes pain and tenderness in muscles we assume that it causes many other If, however, the pain is not ischæmic but neural, we shall have to discard ischæmia as a common of pain

Summary

Ischæmic muscles can be exercised without pain considerable periods if their nerve supply is und

Pain develops in muscles which are worked with blood-supply but with nerves partially blocked

So-called ischæmic pain in muscles is due chiefly fatigue through partial nerve block

Factor P cannot be detected in the circulating blood

There is no evidence that ischæmia is a general of obscure pains

REFERENCES

Addis H St C C, Jepson R P, Kellgren J H (1950) Sci 9 271
Barlow E D, Pochin, E E (1948) *Ibid*, 6, 303
Boyd A M, Ratcliffe A H Jepson, R P, James, G W H (
J Bone Jt Surg 31B, 325
Capps, R B (1941) *Arch intern Med* 68, 94
Gellhorn, E Thompson, L (1944) *Proc Soc exp Biol, N Y*
Gilliatt, R W, Wilson, T G (1953) *Lancet*, ii, 595
Harpuder, K., Stein, I D (1943) *Amer Heart J* 25, 429
Kahlstrom, S C, Burton C C, Phemister, D B (1939)
Gynec Obstet 68, 129
Karl R C, Peabody G E, Wolff H G (1945) *Science*, 102, 1
Kellgren, J H (1938) *Clin Sci* 3, 175
Kelly M (1955) *Neurology* (in the press)
Kugelberg, E (1946) *Brain* 69, 310
Lewis T (1932) *Arch intern Med* 49, 713
— (1936) *Clin Sci* 2, 237
— (1942) Pain New York and London
— Pickering, G W Rothschild P (1931) *Heart*, 16, 1
MacWilliam J A, Webster, W J (1923) *Brit med J* i, 51
Maison G L Forster A C (1938) *Proc Soc exp Biol N Y* 38,
Marshall, J Poole, E W Reynard, W A (1954) *Lancet* i, 1
Merrington, W R. Nathan P W (1949) *J Neurol Psychiat* 1
Nathan P W (1953) *Ibid* 16 144
Ray M B (1934) Rheumatism in General Practice Lond
p 66
Rein, H Schneider M (1937) *Pflüg Arch ges Physiol* 239, 451
Ryle J A (1942) *Guy's Hosp Rep* 91, 147
Sinclair D C (1948) *J Neurophysiol* 11 75
— Weddell, G Feindel, W H (1948) *Brain*, 71, 184
Sunderland, S, Kelly M (1948) *Aust N Z J Surg* 18, 75
Tunis M M, Wolff H G (1954) *Arch Neurol Psychiat* 71, 42
Wikler, A G (1953) *Neurology*, 3, 656
Woodbury R. A., Torpin R, Child, G P, Watson, H, Jarboe,
(1947) *J Amer med Ass* 134, 1081

A CASE OF FAVISM

O R McCarthy
B A, M B Dubl

LATE SENIOR HOUSE PHYSICIAN, ST RICHARD'S H
CHICHESTER

FAVISM is a disease in which acute hæmolysis foll the ingestion of broad beans (*Vicia fava*) or inhala of their pollen It is seen chiefly in Sardinia, but also Sicily, Italy, Greece, and North Africa (Luisada 1 Sporadic cases have been reported from France Spain, 10 have been described in the United (Larkin 1953), and 2 in Britain (Diggle 1953) All th affected were people of Mediterranean ancestry

Symptoms appear 5–24 hours after ingestion of beans, or in a matter of seconds after inhalation of t pollen There is malaise, nausea, and vomiting Pyrex if present, is irregular The patient becomes jaund and his liver and spleen may enlarge There is a in the red-cell count, a rise in serum bilirubin serum-potassium, a reticulocytosis, and often a cytosis The urinary urobilin may increase, and al uria and hæmoglobinuria may be present An m d-cell fragility may be found in the early stages, but ually fragility is normal

The severity varies from the acute case requiring ood transfusion to mild ambulatory cases with few ms. The disease is commonest in male children during e pollen season (May to August) Skin testing with an tract of the bean or pollen gives variable results Each tack is followed by a period of about 6 weeks' immunity om the disease during which time skin tests are gative

The condition is usually regarded as a manifestation allergy, though this is not accepted by all authorities *Journal of Pediatrics* 1954)

Case-record

A 9 year old boy was admitted to hospital on July 2 1954 investigation of recurrent attacks of jaundice

His present illness had begun on June 26 1954 At supper that day he ate some cooked home-grown broad beans d during the evening he felt rather unwell. Next morning ate some more beans, and about 2 hours later he had a ivering attack and felt ill He went to bed early and the llowing morning (June 28) he was found to be jaundiced. o vomited several times during that day and night and en slowly improved By July 1 the jaundice had begun fade

Previous history—He had had jaundice twice before in 952 and in 1953 each time during the late spring Both ttacks were closely preceded by a meal containing broad eans, and each attack consisted in shivering malaise omiting and jaundice Neither had been as severe as e *1954* attack, and on neither occasion was a doctor lled

Family history—His mother volunteered the information at her maternal uncle used to become ill and jaundiced very time he ate broad beans. He was *unmarried* and died ine years ago So far as she knew no-one else in the mily had had recurrent jaundice The patient was born England and had lived all his life in England His parents randparents, and the grand uncle's parents had all been born the British Isles.

On examination he was slightly above average height and eight for his age The scleræ were yellow and the skin ightly so The liver edge was palpable just below the ostal margin, and was tender The *spleen* was not palpable and no other abnormality was found on physical amination.

Blood examination on July 5 showed Hb 74% red cells 400 000 per c.mm reticulocytes 24% and serum bilirubin mg per 100 ml Examination on July 7 showed reticulocytes 10% normal red-cell fragility (hæmolysis starting at 44% and complete at 0 28%) white cells 8700 (polymorphs 0%, lymphocytes 42% monocytes 6% eosinophils 2%) ed cells normal in shape and size and no punctate basophilia. he anti-globulin reaction was negative By July 16 the eticulocytes had dropped to 1 5% Wassermann and Kahn eactions were negative

Other examinations—There was no bilirubin or urobilin in he urine An intradermal skin test on July 15 using an xtract of broad beans was negative

Progress—There was an evening rise of temperature up o 99·6°F for a few days The jaundice cleared within 4 hours of admission There were no further symptoms nd signs, and he was therefore discharged on July 18 having een warned never to eat broad beans again

On Sept 9 he was seen as an outpatient He had remained t in the interval. A further skin test was negative Blood xamination showed Hb 100%, reticulocytes less than 0·2% rum bilirubin 0·8 mg per 100 ml., normal red cells and latelets, and no evidence of spherocytosis.

Discussion

The diagnosis was made (1) on the history of symptoms ppearing within 24 hours of eating broad beans; (2) on he evidence of hæmolysis as shown by the low hæmo lobin the low red-cell count and the high reticulocyte ount; and (3) on the absence of excessive fragility or bnormal shape of the red cells The negative antiglobulin reaction on July 7 was to be expected since the hæmolytic episode was over by that time

This is probably the first case of favism to be described in a person of non Mediterranean descent The diagnosis might not have been made but for the mother's insistence on the connection between the beans and the jaundice (she probably recalled that her uncle had shown a similar susceptibility)

Diggle (1953) has pointed out that where hæmolytic anæmia is found in a person of Mediterranean ancestry, the possibility of favism should be borne in mind. Dacie (1954) noted that in many of the published case-reports on favism, the original diagnosis had been of "acute hæmolytic anæmia—? Lederer's type" the correct diagnosis was made after eliciting a history of recent ingestion of beans

This case suggests that favism should be considered as a cause of hæmolytic anæmia not merely in Mediterranean people or their descendants but also in persons of British stock

Summary

A case of favism is described in an English boy of 9 *This is* the first report of the condition in a patient of British descent There are grounds for believing that the boy's grand uncle had the same disease.

Favism should be considered as a possible cause of hæmolytic anæmia and unexplained jaundice, even in patients who are not of Mediterranean stock.

I am indebted to Dr G A. Emmerson under whom the case was admitted, for permission to publish this report and to Dr G A. Harrison and Dr Colin Knowles, who were responsible for the pathological investigations.

REFERENCES

Dacie J V (1954) The Hæmolytic Anæmias London.
Diggle J H. (1953) *Arch. Dis. Childh* 28, 141
Journal of Pediatrics (1954) 44 606
Larkin V D (1953) *J Pediat* 42, 453.
Luisada A (1941) *Medicine Baltimore* 20 229

PEPTIC ULCER IN A HÆMOPHILIAC TREATED BY GASTRECTOMY

WILLIAM WALKER
M.D Durh.
LECTURER IN CHILD HEALTH UNIVERSITY OF DURHAM

THE danger of bleeding after injury in hæmophilia has long been known and Birch (1937) reported many deaths following even minor surgery

Craddock et al (1948), reviewing the problem of surgery in hæmophilia drew attention to the greater risks of bleeding in cases where local hæmostatic measures could not be applied an arm was successfully amputated in a hæmophiliac but in abdominal surgery the danger of hæmorrhage was so great that many authorities regarded the risks attending infection in acute appendicitis as less serious than those attending operation Craddock et al also described their own *case of acute appendicitis* treated by operation in which the clotting time was kept within normal limits by the use of fresh blood plasma and antihæmophilic globulin and yet the patient died At necropsy blood was found in the peritoneum and pleura and a large hæmatoma not communicating with the peritoneum was found at the site of the incision They calculated that the mortality rate associated with abdominal surgery in probable hæmophilia was at least 27% but where only proved cases of hæmophilia were considered the mortality rate was 60%

I describe here a case of repeated hæmatemeses due to peptic ulcer in a hæmophiliac who subsequently underwent gastrectomy Although the operation was successful I am convinced that surgery in hæmophilia must be avoided if at all possible

Case-report

The patient, who was in his early forties, came from a family of bleeders The family history is typical and illustrates the transmission of hæmophilia by unaffected females to their male children (fig 1) Both the maternal grandfather and a great uncle were said to have died from bleeding, but the exact circumstances are unknown

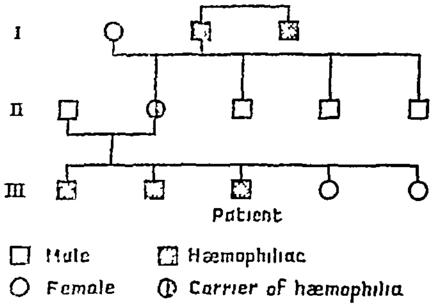

Fig 1—Patient's family tree

History of Bleeding —Although never a florid hæmophiliac the patient has had recurrent epistaxes, skin hæmorrhages, and, at the age of 21, a hæmarthrosis of his left knee Superficial wounds on many occasions bled unduly but never gave rise to anxiety, in fact, severe lacerations did not require any special treatment to produce hæmostasis The bleeding time was repeatedly normal, whereas the clotting time was often prolonged In September, 1952, his clotting time (Lee and White) was 9 minutes (normal 5–10 minutes), bleeding time 2 minutes, clot retraction normal, prothrombin and fibrinogen 93% and 0 2 g per 100 ml respectively, and prothrombin consumption 30% In view of the normal clotting-time specimens of his blood were sent to Dr R G Macfarlane and Dr Rosemary Biggs at the Radcliffe Infirmary, Oxford They confirmed the diagnosis of hæmophilia "Our tests show that he has a definite deficiency of antihæmophilic globulin, in other words he has classical hæmophilia The results cannot at present be expressed quantitatively"

History of Dyspepsia —For 20 years the patient had symptoms typical of duodenal ulcer, which had been repeatedly demonstrated by barium meal 7 years ago he had a perforated duodenal ulcer, which was sutured, fresh blood being given before operation In the seven years from the perforation to the present illness he had eleven hæmatemeses, seven were serious and necessitated admission to hospital and nearly always blood transfusions The amount of blood given varied at first as little as 3 pints was required, but on each of the two most recent admissions—i e, August and October, 1952—more than 20 pints was needed Fresh blood from emergency donors was used whenever possible It was not uncommon for the patient's Hb level to be as low as 4 5 per 100 ml after hæmatemesis The duration of his stays in hospital varied from 10 to 40 days Continuous medical treatment, including prolonged periods of rest, did not produce appreciable improvement, in fact, the hæmatemeses became not only more frequent but also more severe The patient was virtually unemployed, and his family life was becoming disrupted Moreover, Prof F J Nattrass felt that sooner or later the patient would die from a hæmatemesis, and that therefore the considerable risk of gastrectomy was justified

Admission for Gastrectomy —Preparations to control bleeding during and after gastrectomy were made on the assumptions that (1) the clotting defect in hæmophilia is due to the lack of antihæmophilic globulin, (2) provided antihæmophilic globulin can be maintained at an adequate level, the clotting and other hæmostatic mechanisms are normal (3) antihæmophilic globulin is present in freshly collected blood, but after storage its concentration tends to fall (although this is a variable factor), purified antihæmophilic globulin is not available in large quantities and that present as a contaminant of purified fibrinogen has been inconstant and disappointing in controlling bleeding in hæmophilia, (4) antihæmophilic globulin is only effective for 24–48 hours after injection, and is probably much less this (R G Macfarlane personal communication), and (5) relatively large amounts of human blood are necessary to provide enough anti philic globulin to overcome the clotting defect in h (Dacie 1952), and small amounts of blood or plasma recommended by Schiller et al (1948) are unreliable It realised that repeated transfusions of plasma might lose effect as the result of the patient's becoming immunised antihæmophilic globulin, but this risk was unavoidable accepted, as were those of plasma hepatitis, &c

Preoperative Preparation —Twenty emergency blood-do were tested to make sure that their blood was compatible the patient and with each other, and that their plasma promote normal clotting of his blood On the day b operation blood from twelve such donors was colle into acid citrate dextrose solution and within three h transfused into the patient by exchange transfusion. T technique was simple, siliconed giving and taking sets b used to withdraw blood from one arm while the fresh bl was run into the other There were no technical difficult and the rate of bleeding was controlled by altering the tens of the tourniquet, and the rate of infusion by positive press An exchange of 10 pints was completed in 80 minutes, which the remaining 2 pints was run in by slow drip this procedure normal blood was substituted for at least of the patient's blood Perhaps a similar quantitative r might have been achieved by transfusing about five p of fresh plasma However, the exchange transfusion did upset the patient, and since it was completed within an h and a half, he obtained a good night's rest before operation.

Partial gastrectomy was done by Prof Norman Hodg on Jan 26, 1953, at 9 30 A.M, 20 hours after the exch transfusion was completed It would probably have b wiser to operate immediately after the transfusion Dur the operation 1 pint of blood, collected on the previous d from a selected donor, was given There were many m adhesions between the liver and the whole of the curvature than are usually seen after a perforation W these were separated, the stomach was seen to be di The duodenum showed stenosis due to a chronic ulcer in *first part, and was slightly adherent to the pancreas* easily separated The duodenum was divided and cl without difficulty On exposure of the lesser greyish swelling of unknown nature was found and with considerable difficulty, together with the sto An anastomosis was made by bringing the jejunum throu the transverse mesocolon A Penrose drain was *down to the stump of the duodenum, and the a* wall was sutured in layers During the operation the b was no more severe than usual, and the blood appe to coagulate in normal time

Postoperative Course —During that afternoon 1 pint blood, collected on the previous day, was given and fo by 1 pint of saline solution At 6 15 P M the patient v bloodstained material, and thereafter small amounts of bl stained fluid were aspirated from the "stomach"—about every 15 minutes, 33 oz being withdrawn by midni Thereafter the bleeding seemed to increase, because times 4 oz was aspirated in 15 minutes So a tra[illegible] bank blood was started, 2 pints being given over the 6 hours, after which saline solution was substituted for bl (fig 2)

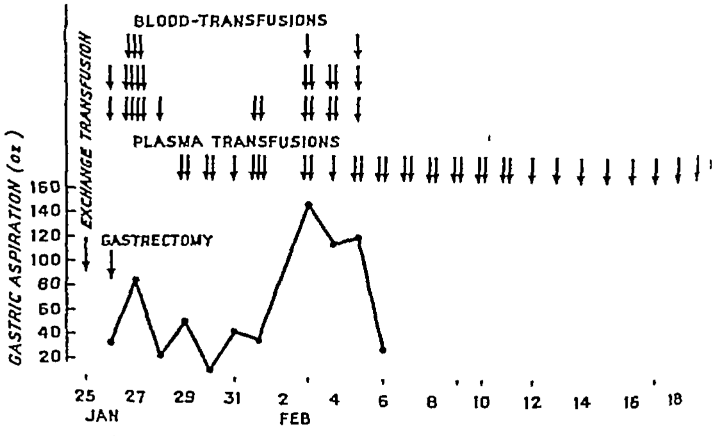

Fig 2—Postoperative course Each arrow represents 1 pint.

Next day 37 oz. of deeply bloodstained material had been aspirated from the stomach since midnight and the patient was in a state of profound circulatory collapse semiconscious, and very apathetic, with pulse-rate 140 and systolic blood pressure 90 mm. Hg A transfusion of bank blood was again started 1 pint being given in 10 minutes and 2 more in the next hour followed by 750 mg of fibrinogen (M.R C Blood Products Unit) which contains antihæmophilic globulin, and by 2 pints of blood freshly collected from specially selected donors The patient improved and was conscious, but with blood pressure 110/70 mm. Hg and pulse-rate 120 Later that day 4 pints of fresh blood was given and a rectal drip of tap-water was started because the patient was becoming dehydrated The stomach was aspirated hourly deeply bloodstained material being obtained on every occasion until 8 and 9 P.M During this day the patient had 84 oz. withdrawn and received 5 pints of bank blood and 6 pints from emergency donors in fact his entire blood volume was replaced. In addition he was given 750 mg of fibrinogen which in antihæmophilic content is said to equal 500 ml of plasma, but in fact is probably equal to only 50 ml of plasma (R G Macfarlane personal communication)

From Jan. 28 to Feb 1 the patient was much better rational, and reasonably coöperative but still very anxious He was given 1 pint of fresh plasma morning and evening—i.e about every 12 hours. The plasma used was of the same ABO and Rh groups as the patient s but not cross matched Freshly collected blood from two donors was centrifuged and the plasma siphoned off and pooled A new drip using a small needle was set up on each occasion the transfusion taking about 20 minutes. During these five days the patient s condition remained satisfactory although about 30 oz of bloodstained fluid was aspirated daily Throughout this time 2 oz of either water or orange-juice was offered each hour On the day of operation the patient took only 2 oz. but next day he took 20 oz and thenceforth he gradually increased his intake to about 60 oz a day

On Feb 1, in addition to the fresh plasma he was given 2 pints of day-old blood to counteract mild anæmia. He seemed well the operation wound was healing normally and there was no bleeding The transfusions were therefore discontinued

Next day his condition was satisfactory and no bleeding occurred but on Feb 3 at 7 15 A.M , 34 hours after the last plasma transfusion, he vomited 18 oz of blood, and 18 oz. more was aspirated in the next 15 minutes so 1 pint of plasma (18 hours old) was given at 9 30 A.M and 1 pint newly collected from emergency donors at 10 A.M In spite of this 20 oz of bloody fluid was being aspirated every half hour the blood pressure was falling and the pulse rate was 120 A transfusion of fresh blood from emergency donors was started at 12.30 P.M 5 pints being given, and 145 oz. of fluid being aspirated from the stomach, during the day

On Feb 4 1 pint of fresh plasma and 4 pints of fresh blood were given and 114 oz aspirated. On Feb 5 1 pint of fresh plasma was given in the morning 3 pints of fresh blood during the day and 1 pint of fresh plasma in the evening ; and 121 oz. was aspirated On Feb 6 the patient s general condition and mental outlook had much improved 1 pint of fresh plasma was given in the morning and at 10 A.M 30 oz. of fluid was withdrawn after which no further aspiration was required Another pint of fresh plasma was given in the evening

From Feb 7 to Feb 11 1 pint of fresh plasma was given each morning and evening On Feb 11 the wound was healing normally and the last of the sutures were removed From Feb 12 to Feb 22 one pint of fresh plasma was given each evening By Feb 12 the patient s weight normally 11 st 4 lb had decreased to 10 st but on this date he started to take food by mouth once more On the six consecutive days up to Feb 22 tests for occult blood were negative. The plasma transfusions were stopped after Feb 22 and there was no further bleeding The patient progressed well and was discharged home on Feb 27 a month after admission during which time he had received 39 pints of blood and 38 pints of fresh plasma. This represents more than 100 donations of blood and but for the donors it is unlikely that he would have survived

Follow up—The patient was seen at monthly intervals for 6 months and apart from a feeling of fullness and some vomiting after meals remained well. His stools were tested for occult blood during the first three months convalescence but were negative on each occasion His appetite was satisfactory he was gaining weight and no anæmia developed Seen in October 1954, 21 months after gastrectomy, he said he felt perfectly well and was doing heavy manual work without difficulty He weighed 11 st 4 lb (his normal weight) and had no complaints.

Discussion

It is difficult to overestimate the risk attending surgery in hæmophilia Even if the clotting time is nearly normal or can be maintained within normal limits by injections of fresh plasma or of antihæmophilic globulin, severe bleeding may still occur (Merskey 1951, Baserga and de Nicola 1951)

Until potent antihæmophilic globulin is available in large amounts fresh plasma is the best means of supportive treatment in the case of accidental injury or if operation cannot be avoided Very large amounts of fresh plasma are required and should be given frequently—e.g every 12 hours—because the active principle survives only a few hours and therefore may fall to dangerously low levels between transfusions Transfusion therapy should be continued as long as there is evidence of bleeding and until it is reasonably certain that healing is well established It is important that during the operation the circulating blood should contain adequate amounts of antihæmophilic-globulin because otherwise arterial hæmorrhage is very likely to recur

Macfarlane et al (1954) have reported the value of bovine and antihæmophilic globulin in patients undergoing surgical treatment, and it seems that this is the real hope for these unfortunate people. At present it is not available in large amounts, and in some cases it seems to carry the risk of producing thrombocytopenia, although in none of these workers cases did this cause bleeding

Any method by which antihæmophilic globulin is introduced into a patient to whom it is a 'foreign protein" carries the risk that the patient may become immunised to it and therefore no longer derive benefit from it.

Summary

A case of repeated hæmatemeses due to duodenal ulcer in a hæmophiliac is reported

Eventually gastrectomy was done The régime before and after operation is described.

The need to avoid major surgery in hæmophilia at practically any cost is emphasised

I am indebted to Professor Nattrass and Professor Hodgson for permission to publish Dr R G Macfarlane and Dr Rosemary Biggs for confirming the diagnosis of hæmophilia the Regional Transfusion Centre for their service ; and the doctors and nurses of the Royal Victoria Infirmary for their skill and care in looking after the patient

REFERENCES

Baserga, A., de Nicola P (1951) *Lancet*, ii 1039
Birch, C L. (1937) Hemophilia Clinical and Genetic Aspects. Urbana, Ill.
Craddock, C. G jun Fenninger L D Simmons B. (1948) *Ann Surg* 128 888
Dacie J V (1952) *Brit med. J* ii, 1408
Macfarlane R. G Biggs R. Bidwell F (1954) *Lancet* i 1316
Merskey C. (1951) *Brit med J* i 906
Schiller F., Neligan G., Budtz-Olsen O (1948) *Lancet* ii 842.

'There is one possible consequence of the use or the testing of thermo-nuclear weapons which is seldom mentioned but which must be in the minds of some biologists It has to do with the effects of radiations upon symbiotic and parasitic organisms Now living things live together in relationships which have themselves become adjusted over long periods of selection. Many trypanosomes, for instance do little harm to the hosts in which they live A mutation in a population of trypanosomes resulting in the production of a new viable form can have very serious consequences for the host population which may be faced with a new situation with which it is not fitted to cope —Prof PAUL G ESPINASSE *Manchester Guardian* March 31 1955

Reviews of Books

British Practice in Radiotherapy

General Editors SIR ERNEST ROCK CARLING, LL D, F.R C S, F.R C P, F F.R, consulting surgeon, Westminster Hospital, B W WINDEYER, M B, D SC, F R C S, F R.A C S, F F R, professor of radiology, University of London, D W SMITHERS, M D, F.R C P, F F R, professor of radiotherapy, University of London London Butterworth 1955 Pp 516 £4 5*s*

SIXTY-FIVE authorities have contributed to this picture of radiotherapy practice in Great Britain today The volume, though complete in itself, is also a companion to *British Surgical Practice*

Part I deals with general problems, including the basic physical aspects, biological problems and effects, and methods of application Part II is concerned with treatment Systematically each chapter deals with a subject for which radiotherapy is used, and its use is discussed fully and clearly by a physician or surgeon and a radiotherapist The necessary and growing coöperation between radiotherapy and other departments is stressed throughout The chapters on cancer of the uterus and breast, on the nose and nasal sinuses, and on chronic rheumatic disease are especially clear and informative The chapter on records and presentation of results is also useful Surprisingly there is no section on the treatment of salivary gland tumours

The diagrams, tables, and illustrations are as clear and lucid as the text This excellent book can be recommended not only to the radiotherapist but to all those who send patients to the radiotherapy department

Human Limbs and their Substitutes

Editors PAUL E KLOPSTEG, PH D, SC D, director of research, Northwestern Technological Institute, Evanston, Ill, PHILIP D WILSON, M.D, surgeon in chief, Hospital for Special Surgery, New York New York and London McGraw Hill 1954 Pp 844 96*s*

UNTIL lately the design, manufacture, and fitting of artificial limbs, and the training of amputees in their use, were in the hands of firms making such appliances and a few limb-fitting surgeons The craft had developed empirically, and though the product was tolerably satisfactory it was without a scientific basis The surgeon-general of the United States army determined at the end of the late war that his pensioners should have the best that man could devise, so he enlisted the aid of the National Research Council The council has carried out one of the most elaborate and comprehensive investigations ever made into a single aspect of human behaviour The scheme, ambitious in conception, and far beyond the scope of individual enterprise, is an outstanding example of the possibilities of research organised at national level and sponsored by national bodies It has covered fundamental research into every aspect of all the problems of the amputee, and it has called for the integrated work of orthopædic surgeons, anatomists, neurologists, psychologists, civil engineers, plastic engineers, physicists, and manufacturers This volume reports the results of seven or eight years' work by the different groups

There are chapters on the mechanics of muscles and of locomotion, new developments in artificial legs, arms, hands, and hooks, the technique of cineplasty, the electric arm, suction sockets, the prescription, alignment, and fitting of prostheses, the evaluation of new devices, and many others *Much of the work is highly technical, it reports basic observa*tions not yet directly applicable to the construction of prostheses, and some which, though still experimental, point the way for future development

Dr Klopsteg and Dr Wilson, an engineer and a surgeon, have done a magnificent job in presenting such a heterogeneous mass of material as a coherent story The [illegible] is indispensable for everyone concerned with [illegible] limbs, and no orthopædic surgeon can afford [illegible] the basic research in human physiology and what it reports

Textbook of the Rheumatic Diseases

2nd ed Editor W S C COPEMAN, O.B E, M.D F R C P, senior physician, Arthur Stanley Institute f Rheumatic Diseases, Middlesex Hospital Edinburgh London E & S Livingstone 1955 Pp 754 52*s* 6*d*

THE first edition of this textbook was published before cortisone and corticotrophin made their début In the second edition the place of these hormones in treatment is considered by several of the 26 contributors who form Dr Copeman's authoritative team

The book is a series of essays, and some overlapping has been accepted and encouraged, thus each section stands by itself as the considered statement of an expert surveying familiar territory, and not subjected to undue editorial restraint The reader in search of a complete picture of the treatment of rheumatoid arthritis must be prepared to wend his way from a general chapter on the disease to others on hydrotherapy, physical medicine, and orthopædics A minor criticism is the mixing of positive and negative reproductions of radiographs throughout the book, even on facing pages The difficult task of surveying the whole subject of the adrenal hormones has been attempted in a new chapter There are some misleading statements in this account, particularly on the effect of adrenal hormones on antibody production and on reactions of hypersensitivity The only work on antibody production cited is the old observation of a rise in titre associated with the lympholysis induced by adrenal stimulation This phenomenon has never been confirmed, and more recent and important work on the depression of antibody production by cortisone is not mentioned. There is some apparent confusion between the effects of cortisone on tuberculin sensitivity and on susceptibility to the spread of tuberculous infection In a short description of collagen diseases "hyaluronidase" is used where hyaluronic acid is intended, and fibrinoid degeneration is rather loosely defined Fortunately a clear and accurate account of connective tissue pathology is included in a separate chapter

This work has deservedly secured its place as a standard textbook, and the appearance of this up-to-date second edition is timely

Insanity, Art and Culture

FRANCIS REITMAN, M.D, D P M Bristol John Wrigl & Sons 1954 Pp 111 12*s* 6*d*

THE influence of a particular culture upon the artist productions of the mentally ill is a special case of tl more general problem of artistic creation in differei societies Dr Reitman has assembled paintings an drawings by psychotic patients in Mexico, East Afric Egypt, India, Ceylon, Japan, and New Zealand, in a these, of course, occidental influences have to be reckone with to some extent in the prevailing culture

The material was not large enough to allow quantitativ analysis, but the qualitative characteristics of schizophreni painting were present in the production of the Egyptian Indian, Sinhalese, and Japanese patients, though some features that would be indicative of illness in a European patient reflected normal cultural forms when they occurred in the production of the oriental patients Dr Reitman then examined the influence of the artistic medium by comparing psychotics' paintings with their needlework and scripture, and he expresses the surprising opinion that "in our present day cultural pattern there seems to be little to stimulate activity in any visual art other than painting" In succeeding chapters there are brief accounts of the lives of Alfred Kubin and George Morland in relation to their artistic activity, some reflections on drawings and paintings carried out "automatically" as in a trance or while doodling, and a somewhat irrelevant sketch of Mytton, the well known eccentric The book, which contains suggestive ideas about the diagnostic value and the complex sources of artistic production, would gain by a fuller consideration of some previous writings, such as those of Kreyenberg, Morgenthaler, and Pfeifer

Proceedings of the International Congress of Physical Medicine—The proceedings of this congress, which was held in London in July, 1952, have now appeared Copies (30*s* post free) may be had from the International Federation of Physical Medicine, 45, Lincoln's Inn Fields, London, W C 2

THE LANCET

LONDON SATURDAY, APRIL 9, 1955

Mental Nursing Analysed

Bethlem Royal Hospital and the Maudsley together orm a centre of teaching and research so outstanding hat one might suppose they would never want for nursing staff Yet the recruitment problems which re so acute throughout the mental service have affected them too, and in 1951 the board of governors of the joint hospital arranged for a job analysis of their nurses' work. Their aim was to gain information that would help them in formulating their nursing policy and training procedures and the results of the analysis (which was made in 1951–52) have led them to make considerable changes Believing that the findings can be of use to other mental hospitals, they now with great public spirit, present a condensed report[1] of this the first inquiry of its kind into the work of mental nurses Like the Nuffield[2] job analysis of the work of general nurses, it brings its shocks and if, in drawing attention to these we seem to criticise the practice of these hospitals it must be borne in mind that it is their *former* practice that is under discussion and moreover that the training given to nurses in them, even before 1951–52, was probably better than that given in many other mental hospitals now

The most striking finding of the Nuffield report was that three-quarters of the nursing in general hospitals was being done by student nurses, and this new report shows that in mental hospitals too, a large part of the care of patients falls to unqualified nurses

Nurses are classed as ward sister or charge male nurse; senior nurse (either a staff nurse or a student nurse in her last year of training who is second in charge the ward) middle-rank nurse; junior nurse (the oungest in experience on the ward) and part-time urse Their tasks are grouped under the headings are of patients supervision; household duties (among hich are included somewhat surprisingly, bedmaking nd the serving of meals and drinks); duty room work hat is, the writing of reports and notes) and reception nd management. At the time of the survey sisters pent the largest slice of their lives on the last of these 41% of their time at the Maudsley and 34% at Bethlem) he figures for care and supervision of patients by sisters n the two hospitals were only 12% (Maudsley) and 80% Bethlem) Senior nurses spent 15–17% of their time on eception and management but the amounts they pent on care and supervision of patients were strikingly ifferent in the two hospitals—22% at the Maudsley nd 58% at Bethlem Middle-rank nurses had a similar attern spending 7–10% on reception and management nd 48% (Maudsley) and 61% (Bethlem) on care and upervision Junior nurses spent only 5–6% of their ime on reception and management but 42–51% on are and supervision of patients The number of hours worked by part time nurses differed considerably in the wo hospitals Though some of them were trained nurses they spent much time on household duties (44% at Bethlem 57% at the Maudsley) At Bethlem most of their remaining time went on care and supervision of patients but at the Maudsley only a quarter of their time was spent in this way

From the standpoint of the hospitals, there was nothing much wrong with the arrangement whereby the nurses who spent most time with the patients were those of the middle and junior ranks, and (at the Maudsley) part-time nurses. Patients need sympathetic company, which kindly young people are quite able to supply, the technical aspect of treatment is in the hands of the doctors, and any junior nurses who have the care of patients recovering from physical treatment learn from their seniors what is required of them On the other hand, the young girl—and even the young man—without previous nursing experience may see the situation rather differently Lay people, among whom untrained entrants must be classed, are ill at ease with those they suppose to be mentally disordered, and the new nurse needs a brief course to orient her to her work—some guidance, for example, in recognising guilt and anxiety, and some notion of the ways in which these are augmented or reduced Admittedly, during her 8 weeks in the preliminary training school (P.T.S.) she would hear the sister tutor lecture (for about 1½ periods a week, usually on Saturdays) on various aspects of mental illness, but the official syllabus for the preliminary State examination, to which the course otherwise adhered contains no mention of psychology or psychiatry In any case, even at Bethlem and the Maudsley new nurses did not necessarily begin their training in the P.T.S but might reach it only after several weeks, or even months of work in the wards. To have to deal with mental patients without sufficient preparation must be for many people an alarming experience—not because the patients are alarming (they so seldom are) but because of the sense of inadequacy that ignorance engenders Can we doubt that this abrupt introduction to the work was among the chief causes for the loss of 65–70% of student nurses before the end of training most of them during their first year?

Apart from the lectures they attended in the P.T.S., student nurses were offered, during their first year in hospital, 24 lectures on anatomy and physiology by the medical staff, adequate revision classes (some optional, some compulsory) and 6 lectures on psychology from the sister tutor The famous Dr Arnold of Rugby wears in his portrait a puzzled expression which Lytton Strachey attributed to the failure of his boys to make headway in French despite half an hour's instruction in that language every week Do the sister tutors in our mental hospitals acquire a similar look? Or is theirs a look of despair, directed at the medical staff? For a full dress course of 20 lectures on psychiatry and 20 on neurology, from doctors, student nurses had to wait until their second year—and many of them did not wait In their third year they got, also from doctors, 10 lectures on normal psychology (surely rather late in the day), and 6 on child psychiatry and the sister tutor followed up each of these in a discussion period Thus in their second and third years the student mental nurses were having a formal educational diet relatively rich in the nutrients they had been needing all along In some ways however, it was a feast of Tantalus for their attendance at lectures often depended on whether or not they could be spared from the wards Lecture attendance, as a proportion of the possible or ideal, was 56% at Bethlem and 63% at the Maudsley over four years , and of those nurses who were absent, just under half were away for reasons accepted as unavoidable Naturally the student also got a good deal of practical and informal training in the wards, and it was in fact the firm intention at both hospitals that some of this should be given by the doctors Thus there were weekly “ ward talks ” in which the registrar or senior house-officer spent an hour discussing one or more patients with as many nurses as could be spared from the ward at the time But unfortunately at busy moments such engagements are liable to be cancelled, and audiences are seldom at full strength thus at Bethlem, in the year under review, only 53% of the possible number of talks had been given, and student nurses had attended only 32% of those provided for them Students certainly could not count on hearing an informative discussion on all of the cases which came under their care , and they had little opportunity to ask about them at other times for the job analysis shows that they spent only 1–2% of their time with doctors—usually in looking for a patient This need was to some extent met by another means of communication—the “ nurses' notes ” On the admission of a new patient, the registrar wrote his instructions on a sheet with this heading, and the nurse to whom the patient was assigned wrote on this sheet her observations on the patient's behaviour during the week The ward sister handed the notes to the registrar weekly, and he added his own notes and comments Fully used, this is a valuable device , but if (as sometimes) it is neglected the nurse loses interest, and her notes become desultory Registrars and senior house-officers, on appointment, were given a 2½-day induction course, which included a 30 minute talk from the sister-tutor on the part they were expected to play in the training of nurses But these occasions, too, may have helped to stamp the sister-tutors with a look of Dr ARNOLD

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[1] The Function and Training of Mental Nurses. By A. N. Oppenheim with the assistance of Henry Froman London Chapman & Hall on behalf of the Bethlem Royal and the Maudsley Hospitals 1955 Pp. 85. 12s 6d

[2] The Work of Nurses in Hospital Wards London The Nuffield Provincial Hospitals Trust 1953 See *Lancet* 1953, i, 370

The doctors, however, were not entirely to blame if they occasionally displayed only a lukewarm interest in nurse training , for the nursing candidates were of very uneven quality Actually of those who asked for an application form, 70% never filled it in and sent it back , 40% of those who did send it had to be rejected , and two-thirds of those accepted dropped out, most of them during their first year Doctors with more urgent things on their minds may well grudge spending teaching time on young people who are never going to make nurses Nevertheless these things cut both ways a high rate of wastage is a bad advertisement for mental nursing , and a doctor's casual attitude towards nurse training may lose some promising, as well as some unpromising, students In the case of a male student nurse already perhaps worried about the financial prospects, it may make the difference between staying and going , and the disappointment of the good and promising nurse who gives up training may deter many other likely candidates

The survey should encourage mental hospitals elsewhere to consider how far, as employers, they now show themselves skilled in industrial psychology An application form which puts off 70% of candidates might well need revision , and it can be very unwise to plunge an adolescent student, without due preparation, into an environment which is bound at the outset stressful If her further experience of hospital to build up her morale—and that pretty quickly—she is naturally going to leave The makes the practical suggestion that every su nurse might be attached to a psychiatric firm would not only help her to think of herself as part team, but might help the doctors, too, to think of in this way, and to treat her accordingly

Chelating Agents

TREATMENT of metallic poisoning by chelat agents was introduced a few years ago in the Unit States by BESSMAN and his colleagues,[1] and ma reports have since testified to the value of this metho Earlier this year we published an account of a ca of lead poisoning in a child successfully treated by th chelating agent, calcium disodium ethylenediam tetra-acetic acid (E D T.A)[2], and on a later page this issue Professor BROWNE describes two cases adults

Chelating agents (χηλή, a claw) combine wi certain metals to form firm complexes They ha this property because they contain nitrogen or oth atoms capable of donating electrons to metals wh require these in order to complete their atomic co figuration The resulting ring structures are ver stable, and the metal is non-ionised and thus do not show its usual chemical or physiological activit Hæmoglobin is a chelated complex containing iro Chelating agents are useful in medicine because th metal complex formed is soluble, is readily excret by the kidney, and is non-toxic the action of chelating agent in metallic poisoning might be likene to that of a policeman peacefully escorting a troubl maker from a political gathering The affinity for th chelating agent varies between the different metals and one metal which forms a stable complex ca displace a second metal whose complex is less stabl This is the basis of the therapeutic use of calciu disodium E D T A in lead poisoning The disodiu salt itself is unsuitable for the treatment of heav metal poisoning, because it very readily combin with calcium,[4] and may thus provoke dangero hypocalcæmia But the affinity of lead for E D T is greater than that of calcium, so administration o the calcium chelate results in lead being safely remov from the tissues

Rational therapeutic use of calcium disodiu E D T A requires knowledge of the pharmacolog of this agent It can be given by mouth, since it absorbed to some extent from the gut without significantly chelating metals present in the alimentar tract[5–7], but absorption is greater when it is giv subcutaneously[8,9] or intravenously E D T.A rapidly excreted unchanged in the urine, about 90 of the dose being eliminated within six hours aft intravenous injection[10] At the pH of the bod 1 molecule of lead is bound to 1 molecule of E D T If the chelating agent were fully efficient in the bod

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1 Bessman S P Reid H Rubin M. *Med Ann D C* 1 21 312
2 Giles H McC Moore, C J , Still B M *Lancet*, Jan. 22, 19 p 183
3 Martell A E Calvin M The Chemistry of the Metal-che Compounds New York, 1952
4 Spencer, H Vankinscott V Lewin, I , Laszlo D *J c Invest* 1952 31 1023
5 Sidbury J B Bynum J C Fetz, L L *Proc Soc exp B* N Y 1953 82 226
6 Bradley J E Powell, A M *J Pediat* 1954 45 297
7 Cotter L H *J Amer med Ass* 1954 156, 906
8 Bessman S P Rubin M Leikin S *Pediatrics* 1954 14, 20
9 Kneller L A Uhl H S M Brem J *New Engl J M* 1955 252 338
10 Foreman H Vier, M Magee, M *J biol Chem* 1953, 203, 1

3 millimols of calcium E D T.A, equivalent to 5 g, would produce excretion of about 260 mg of lead The figure observed by **Bessman** et al[8] was in fact only 1 8 mg of lead representing an efficiency of 0 7% The probable reason for this low efficiency is that lead is bound in the tissues to sulphydryl groups, and although the affinity of lead for calcium E D T.A. is greater than it is for the SH groupings, these are much more numerous in the tissues **Bessman** et al found that increasing the dose of calcium E D T A. did not increase the excretion of lead probably because much of the larger dose is excreted in the urine before it can be brought into equilibrium with the tissues This would suggest that the best way to give calcium E D T.A in acute lead poisoning is by slow continuous infusion or by repeated infusions, and hitherto the latter method has been the most commonly used A single dose need not exceed 0 5 g, this amount is usually given dissolved in about 200 ml. of saline over a period of two hours, and infusions are repeated every eight or twelve hours for about five days Subsequent courses of similar duration are given, divided by intervals of a few days Administration of the chelating agent is rapidly followed by a large excretion of lead chelate in the urine, with a daily output of up to 4 mg, the blood lead level falls steadily, symptoms of acute lead poisoning are rapidly relieved[11], and over a period of days coproporphyrin disappears from the urine, the stipple cell count in the blood falls to zero, the lead line in the gums disappears, and the dense band at the metaphysis of the long bones of children becomes no longer demonstrable radiographically The oral preparation is probably best reserved for the treatment of less acute cases[8] There is evidence that calcium E D T.A can be given safely the vital elements iron, copper and cobalt, do not displace calcium from the calcium E D T.A complex serum levels of sodium and magnesium are not seriously deranged[7], and the serum calcium level itself remains unaffected[4] The lead E D T.A complex has caused few side-effects[7]

E D T.A. has also been used in the treatment of poisoning due to other heavy metals for example, **Maloof**[12] found that an ointment containing calcium disodium E.D T.A is of value against the indolent chrome ulcers seen in the tanning industry But this agent may have *further* uses In laboratory animals it removes radioactive isotopes, such as yttrium[13]—a property that *may prove* clinically important. In a different approach, an attempt has been made to "chelate" out of the body calcium which has accumulated in pathological processes such as nephrocalcinosis, otosclerosis, peripheral vascular disease and calcified mitral stenosis[14] The theoretical justification for such a measure has not yet been fully worked out, nor *is this measure* free from hazard In two cases of hypercalcæmia treated with sodium E D T.A by **Dudley** *and his* colleagues[15] the patients died and necropsy revealed severe damage in the proximal convoluted tubules of the kidneys, which **Dudley** et al believe was probably a result of the therapy

In E D T.A. the physician has acquired a valuable and safe means of treating acute and chronic poisoning by various heavy metals, and a chemical tool which, if used judiciously, may lead to better understanding of many metabolic problems

Ascites

The development of *ascites in portal cirrhosis* of the liver depends on several factors, but the movement of fluid from the capillaries into the peritoneal cavity is controlled primarily by hydrostatic and colloid-osmotic pressures[1] Tending to force fluid out of the vascular compartment is the capillary blood pressure and drawing it out is the osmotic pressure of the proteins in the interstitial and ascitic fluid An opposing force is exerted by the osmotic pressure of the plasma-proteins, and by the intra-abdominal hydrostatic pressure

Portal cirrhosis increases the resistance to blood flow through the liver[2], and this in turn increases *the portal venous* pressure, which has *been measured* directly at operation, by determining the pressure in portal collateral veins as they run up the anterior abdominal wall, and by passing a catheter via the right atrium into a hepatic vein. If the catheter is inserted until it occludes the vein the pressure recorded agrees closely with the portal venous pressure—the technique is analogous to measuring the left atrial pressure by wedging a catheter in a pulmonary arteriole[3] By this means **Sherlock** *and her* associates[4] found that the portal venous pressure averaged 7 mm Hg (range 2·6–11 2) in healthy people and was raised *to* 22 (range 15 6–35 2) in 11 patients with cirrhosis By *itself* increased portal venous pressure does *not* cause ascites Ligation of the portal vein in laboratory animals and during removal of the pancreas in man *does not* produce ascites in animals ascites follows only if plasmapheresis is carried out in addition,[5] and *in* patients with extrahepatic portal obstruction ascites develops only when hæmorrhage from œsophageal varices reduces the plasma protein level, when the proteins are restored to normal *the ascites disappears* although the *portal hyper*tension persists Thus a reduction in plasma-proteins as well as *portal* hypertension is necessary for the formation of *ascites*, and in cirrhosis hepatic synthesis of plasma proteins is impaired **Post** and **Patek**[6] have found *fairly close* agreement between the plasma-albumin value and the presence or absence of ascites, the critical level being about 3 1 g. albumin per 100 ml., below which ascites is usually present

In addition to these *two main factors others are* involved, and, although some workers have sought to show that these are primary, most believe that they operate secondarily to the changes in body water and electrolytes that follow the accumulation of several litres of additional extracellular fluid This fluid is derived from the vascular compartment, and unless salt and water are retained the plasma volume will become seriously reduced Thus ascites is associated with a pronounced reduction in the urinary excretion of sodium Since low sodium excretion is at the same time found in saliva, sweat, and fæces and can be reproduced by administration of deoxycortone, it has been suggested that secretion of a mineralocorticoid hormone by the adrenal cortex increases in response to the threat of plasma sodium depletion LUETSCHER and JOHNSON[7] have now confirmed that in cirrhotics with ascites increased amounts of a potent sodium-retaining hormone, aldosterone, are present in the urine In experimental ascites in the dog removal of the adrenal glands is followed by profound sodium diuresis and disappearance of the peritoneal fluid[8], and MARSON[9] has reported a similar response in a cirrhotic patient subjected to total adrenalectomy In addition to aldosterone other adrenocortical steroids may play a part in the conservation of sodium Although the plasma level of 17-hydroxycorticosteroid compounds is not abnormally raised in cirrhosis, there is good evidence that they are not metabolised at a normal rate by the damaged liver[10] Thus the proportion of steroid present in the plasma in an active form, rather than as an inactive conjugate, may be greater than normal although the total amount of unconjugated and conjugated hormone may be no greater than in health Since the plasma-sodium level is not raised in patients with ascites there must be increased retention of water in parallel with the sodium retention Some workers[11] claim to have demonstrated increased amounts of an antidiuretic substance in the urine of such patients, and have suggested that increased secretion, or decreased destruction, of the posterior-pituitary antidiuretic hormone may have a primary rôle in the pathogenesis of ascites Unfortunately the techniques for estimating the antidiuretic hormone in urine are imperfect, and in a careful study WHITE et al[12] have found that cirrhotic patients metabolise antidiuretic hormone at the same rate as healthy people, and other workers with improved techniques have not found that the plasma level of antidiuretic hormone is raised[13] Diminished renal blood-flow has been reported in some[14] but not all[15] patients with ascites, and it seems likely that this, like increased secretion of aldosterone, is a secondary event depending on reduction in effective plasma volume as a result of movement of fluid from the vascular compartment into the peritoneal cavity It is wrong to think of ascites as a static collection of fluid separated from the vascular compartment Studies with radioactive isotopes[16] have shown that within the course of an hour half the ascitic fluid is exchanged with plasma fluid, and albumin given intravenously to raise the plasma osmotic pressure fails to achieve its purpose because the protein passes rapidly into the ascites[17]

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[11] Wade J F, Burnum J F *Ann. intern Med* 1955 42 251
[12] Maloof C C. *Arch industr Hlth*, 1955 11 123
[13] Vaughan J M Tutt M L *Lancet* 1953 ii 856
[14] Clarke N E Clarke C N Mosher R E *Amer J med Sci* 1955 229, 142
[15] Dudley H R, Ritchie A C Schilling A., Baker W H *New Engl J Med* 1955 252 331

[1] Starling E. H *J Physiol* 1896 19 312
[2] See *Lancet* 1954 ii 1316
[3] Hellems H K Haynes F W Dexter L. *J appl Physiol* 1949 2 [illegible]
[4] Paton A., Reynolds T B., Sherlock S *Lancet* 1953, i 918
Reynolds T B., Balfour D C, Levinson D C., Mikkelsen W P Pattison A C *J clin Invest* 1955 34, 213.
[5] Volwiler W., Grindlay J H Bollman J L *Gastroenterology* 1950, 14, 40
[6] Post J Patek A J *Arch. intern. Med.* 1942 69 67

Treatment is aimed at improving liver and sometimes in ascites of sudden onset the may lose a lot of fluid when put to bed on a balanced diet containing 80–100 g protein however, little can be done to improve the state the liver, and treatment is then directed sodium retention by restricting the intake of salt less than 1 g daily[18] An initial paracentesis hasten relief, but repeated paracenteses are to be avoided on account of the large amount of lost to the body If the ascites is not controlled a low-sodium diet alone, mercurial diuretics ammonium chloride should be given twice weekly

Annotations

BCG

THE problems associated with B C G vaccination increasing A preliminary assessment of the vaccinat programme in India, sponsored by the government India and carried out by W H O,[19] *underlines* important points First, owing to the high prevalence non tuberculous tuberculin sensitivity in certain the uninfected cannot be accurately distinguished the infected A varying proportion of children have not been infected by tuberculosis are being exc from vaccination, the proportion probably being as as 50% in some areas Raising the arbitrary limit f positive reaction would bring in more of these but it would also involve vaccination of more of already infected Secondly, the degree of skin after vaccination was found to vary considerably, and many instances was much lower than had been exp It was thought that this could not be due to a rac incapacity of Indian children to develop high sens or to impairment of the vaccine's potency by expos to light Some other factors in its handling or ad tration must have been involved, or there may have inaccuracies in the tuberculin testing The potency tuberculin, like that of B C G, decreases with exposure sunlight[21] *Exposure to subtropical sunlight of a 5* dilution of P P D in clear glass bottles for twelve ho impairs its potency by about 80%

It is important to know what degree of sensitivit being produced by vaccination In vaccinated guineap the length of survival after infection by virulent bacill related to the size of the post vaccination tuber reaction[22] As the dose of living B C G is increased, th is not only an increase in the size of the vaccination le and the subsequent tuberculin reaction, but also survival after infection Heat killed B C G, on the ot hand, leads to small reactions and short surviv although the vaccination lesions are as large as wh living B C G is used The size of the vaccination lesion clearly not a reliable guide to the immunity induc but that of the post vaccination tuberculin reac may be -

The frequency of suppurative lymphadenitis in newborn is causing some concern There are reports an incidence as high as 23% in Taiwan[23] and of 12% in this country[24] The frequency of local absces the site of injection depends largely on the technique vaccination, the deeper the injection the greater risk of an abscess The presence of lymph nodes is apparently unrelated to the severity of vaccination lesion[23] On the other hand, it is clo

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7 Luetscher J A Johnson B B *J clin Invest* 1954 33 1441
8 Davis J O Howell, D S Southworth J L *Circulation Res* 1953 1, 260
9 Marson F G W *Lancet* 1954 ii, 847
10 Brown H Willardson D G, Samuels L T, Tyler F H *J clin Invest* 1954 33 1524
11 Hall C A Frame B Drill V A *Endocrinology* 1949, 44 76 Sims J L *J Lab clin Med* 1950 36 990
12 White A G Rubin, G, Leiter L *J clin Invest* 1951, 30 1287
13 Stein, M, Schwartz, L Mirsky L A *Ibid* 1954 33 77
14 Leslie S H Johnston B, Ralli E P *Ibid* 1951 30, 1200
15 Goodyer, A V N Relman A S, Lawrason, F D, Epstein, F H *Ibid* 1950 29 973
16 Prentice T C Siri W Joiner F E *Amer J Med* 1952, 68 See *Lancet* 1951 i 584
A J Mankin H Colcher, H, Lowell, A., Earle, D P n *Invest* 1948 27, 135

18 Atkinson M Paton A, Sherlock, S *Lancet*, 1954, i, 1
19 *Bull Wld Hlth Org* 1955 12 102
20 See *Lancet* March 26 1955 p 659
21 *Bull Wld Hlth Org* 1955 12, 179
22 *Ibid* p 31
23 Hsing C T *Ibid* 1954 11 1023
24 Gaisford W Griffiths, M *Tubercle*, 1954, 35, 7

lated to the dose of the vaccine and the age of the ild[25] Gaisford and Griffiths[24] found that the incidence as reduced from 11 7 to 0 3% by lowering the dose B C G from 0 2 to 0 05 ml But since the degree immunity may be directly related to the dose of C G[22] the dose should be as large as possible.

A much more serious complication of vaccination has een recorded Meyer[26] reports from Denmark the death f a 9 year-old boy from widespread tuberculosis involv ng the lymphatic system two years after vaccination hirteen cultures of tubercle bacilli were obtained at ifferent times from different lesions before and after eath These were found to be indistinguishable from C.G no normally virulent bacilli were isolated The onclusion that the disseminated tuberculosis and death ere due to the B C.G vaccination is inescapable A imilar case has occurred in Norway[27–29] A man aged 24 ho had been vaccinated four and a half years previously ied after a protracted illness during which there were uberculous lesions in the lymph nodes bones lungs rinary tract, and rectum *Bacilli indistinguishable from* C G were recovered during life and from several organs fter death There is no evidence in either case that the atch of vaccine used was in any way abnormal There ave, of course been previous reports of deaths attributed B C.G —such as those in Hungary in 1930[30 31]—but n none has the evidence been completely convincing t must now be admitted that B C G can cause dis eminated progressive disease in man without any pparent change in its properties in the laboratory ut it is also clear that this must happen very rarely ideed Irvine[32] in 1949 estimated that if all the uspicious cases were included the incidence was less than per million *Between 1951 and 1953 16 million* were accinated in the mass vaccination campaigns of W H O lone[33] and no deaths have so far been reported.

These two deaths do not by themselves give cause to lter the current practice of B C G vaccination Indeed ere is reason to wish that it were more ready obtainable this country by doctors who want to use it At present s import and distribution are closely controlled by e Ministry of Health and only those belonging to rtain specified groups can be vaccinated Such a utious policy may be correct if vaccination is regarded a public health measure But B C G vaccination also oncerns individuals Other protective inoculations are controlled whether or not they are considered by the inistry to be desirable The doctor is free to decide hether the patient for whose health he bears a more rect responsibility than do the public-health authorities, ould be inoculated against, for instance yellow fever e fact that such inoculation is wholly unnecessary in is country is irrelevant But he cannot decide whether e patient should have B C.G If control were removed is unlikely that B C G would in fact be used much more tensively than at present But an important principle ould have been upheld

A NEW MORPHINE ANTAGONIST

Most *clinicians have had to face the problem of* e patient with intractable pain who needs increasing es of morphine which cause severe depression. Shaw d Shulman[34] have given a synthetic morphine tagonist *2–4 diamino 5 phenyl thiazole by injection* doses of up to 40 mg to five patients in the terminal ages of carcinoma. This had the effect of relieving the severe respiratory depression and narcosis induced by the large amounts of morphine which these patients were receiving—up to gr $1^1/_2$ (24 mg) in a single dose—without impairing the analgesic action No disagreeable side effects were noted. This compound differs from nalorphine in that it does not provoke withdrawal symptoms in patients already receiving morphine

THE FIRST TEN MINUTES

The notable reduction in infant mortality during late years has been largely due to decreased mortality in the group aged 1–12 months, as has been shown graphically by Dr Morris and Mr Heady[1] Donald[2] contends that many deaths in the first month are preventable In the past most such deaths were attributed to prematurity, and some progress has been made towards averting premature delivery (Hamlin's work[3] on the prevention of pre eclampsia is a notable contribution) But lately attention has been directed to improving the survival rate of premature babies, in the belief that prematurity is sometimes inevitable Potter[4] has laid down a challenge to clinicians by refusing to accept without close scrutiny prematurity as a cause of death per se in babies weighing over 1000 g (2 2 lb) She states emphatically that the commonest cause of death in premature babies above this weight is hyaline membrane, and though our know ledge of this condition is still imperfect it is probably to some extent preventable and treatable.[5]

If the neonatal survival rate is to be increased then methods of resuscitation and of care of the newborn must be improved One measure which has brought great benefit is the intra gastric administration of oxygen[6] which has been widely practised with excellent results. Atlee[7] urging the need *for closer attention to* the infant in the first minutes after birth writes

> What seems to happen so often is this : immediately the baby is born its cord is clamped and cut, it is handed to a nurse who puts it in a cot at the far corner of the delivery room or in one actually outside the delivery room, while the obstetrician proceeds to sew up the episiotomy Presently someone comes in to say that the baby is either not breathing well or has stopped breathing After that a nerve-wracking 10 or 15 minutes of resuscitation ensues, until the grey blue baby responds sometimes it doesn t

Atlee admonishes us not to let the baby out *of our* hands until it is breathing properly and has a good pink colour all over its body ' He believes that complete drainage of amniotic fluid from the respiratory tract is essential and to achieve this he holds the newborn baby upside down for 5 minutes Gibberd[8] too emphasises the importance of complete removal of amniotic fluid Atlee remarks that the umbilical cord should not be severed until the *infant has received all the* blood from the placenta The advantages of this are clear and are especially great in the case of the premature baby He also suggests that the cord should be tied with tape *thus averting the risk of cord hæmorrhage* associated with clamping He likes to have beside the delivery bed a light carriage in which the baby is kept under the eye of the obstetrician for the all important first few *minutes.* Duckman et al[9] *point out that the baby* should lie at a lower level than the mother Atlee is in fact urging a change of emphasis in the third stage of labour He suggests that obstetricians have concentrated too *closely on the condition* of the mother because of fear of hæmorrhage Nowadays with recourse where necessary to ergometrine the obstetrician should be able to control the third stage without losing sight of the child

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ull *Wld Hlth Org* 1955 12 143
oyer J *Amer Rev Tuberc* 1954 70, 40
hrap Meyer, H *Acta tuberc Scand* 1954 29 173
eding P., Hesselberg I *Ibid*, p 180
aaler E, Oeding I *Ibid* p 188
ardi J, Gorgely J Sureng L. *Gyógyászat* 1930 75 442
ancet 1930 i 1313
rvine K N BCG Vaccination in Theory and Practice London, 1949
ull Wld Hlth Org 1955 12 301
haw F H Shulman, A *Nature Lond* 1955 175 388

[1] Morris, J N Heady J A *Lancet* Feb 12 1955 p 313.
[2] Donald I *J Obstet Gynæc Brit Emp* 1954 61 725.
[3] Hamlin R H J *Lancet* 1952 i 64
[4] Potter E L *J Amer med Ass* 1954 156 1171
[5] See *Lancet* March 19 1955 p 601
[6] Akerren, Y, Fürstenberg N *J Obstet Gynæc., Brit Emp* 1950 57 705
[7] Atlee H B *Canad med Ass J* 1954 70 227
[8] Gibberd, G F Anoxia of the New born Infant Oxford 1953
[9] Duckman, S et al. *Amer J Obstet Gynec* 1953 66 1214

Special Articles

TALK, TACT, AND TREATMENT*

RICHARD ASHER
M.D Lond, F.R C P
PHYSICIAN TO THE CENTRAL MIDDLESEX HOSPITAL

I AGREE with Dr Balint that many doctors select the physical and eschew the psychological factors in their patients' illnesses I know I am as guilty of this as are most physicians All the same, we have some excuse, some reason, for being frightened or suspicious of the subject of psychiatry even though we know that psychological factors are important

Psychiatry seems to me to differ from medicine in having a closer resemblance to religion Beliefs and dogmas are promulgated by certain masters—Freud, Adler, Jung, and so on—and these ideas are believed more from reverence of their originator than from repeated experimental observation Secondly, the language of psychiatry, like that of religion, is often esoteric and concerns itself with concepts and abstractions whose exact meaning is less precisely comprehended than are the majority of medical concepts If for a moment we consider the dynamic formulation of both objective and subjective thought fantasy, then cognitive functions can easily become projected into an integrated but psychically barren wish fulfilment That last high-sounding sentence, as I hope you noticed, has no meaning whatever and is pure nonsense, but I wrote it to demonstrate that with the aid of abstract terms it is easy to parade such a brave show of words in front of one's thoughts that it is extremely difficult to see if there is any idea behind them, and it is equally easy to take a small idea and wrap around it such a glittering mantle of language that it can dazzle the unwary into applause Thus although much wisdom is written by psychiatrists, the nature of the subject and its language make it hard for the ordinary doctor to distinguish the profound from the profuse

Another difference between psychiatry and medicine is that it is easier to prove the correctness or otherwise of medical ideas Modern medicine consists to a large extent in debunking the ideas erroneously held by others We used to treat bloodless limbs by warming them—now we cool them, we used to treat bleeding ulcers by starving them—now we feed them With psychiatric beliefs experimental proof is much harder I have recently been reading the views of psychiatrists on the syndrome of depersonalisation Gordon describes the syndrome as a converted representation of hidden or repressed emotional consciousness by special determination Perhaps he is right, but Schilder stresses the shift of the libido and its partial concentration on a scrutinising tendency Here I find myself asking how one can tell if a libido has shifted and what means are there of assessing its scrutinising tendency Sodger says it may be an attempt to escape psychic castration Perhaps it may, but for a physician the phenomenon of psychic castration is so much harder to understand than is its physical counterpart Wittels says it is caused by an unusually large number of phantom figures leaving the ego undecided about which figure should be acknowledged as its representative As a physician I find myself in complete ignorance as to what is a normal healthy number of phantom figures, would five or six, for instance, be considered excessive ?

I have made these few comments to show how sea the physician feels when he looks at ps theory, and how bewildered he becomes if he how to prove which theory is right

After this rather lame excuse for the ph neglect of psychiatry I will get down to the body of my subject

THE DOCTOR AS A DRUG

Dr Balint spoke of the discovery of his seminar th by far the most frequently used drug in general was the doctor himself "it was not only the med in the bottle, or the pills in the box, that mattered the way the doctor gave them" Here I am in agreement In the words of a popular song "It's what you do, but the way that you do it" Dr continuing the analogy of drug and doctor, regrets textbooks and lecturers teach us the way to use but not the way to use ourselves Admittedly the we deal with our patients, and especially how we to them, is about the most important part of our but can it be taught ? I doubt it It can be experience and to some extent by watching great d handling their patients, but it cannot be taught pharmacology All the power of tongue and pen, all the wisdom of textbook and lecture, can never a doctor the knowledge of when to probe and when leave alone, when to chide and when to reassure, wher speak and when to keep silent They are private with a different solution for every one of the m permutations of personality involved between a and his patient

I believe the analogy between drugs and doctors false one there is such a great difference between Drugs can be standardised and doctors (thank cannot —If you give a man a pill there are only things he can do with it he can swallow it or he throw it away If you give a man explanation or there are uncountable ways of giving it and even ways in which it can be taken Dr Balint tilts at suggestion that common sense and experience will the doctor know how to prescribe himself (in fact ho talk to his patients) and says the shallowness of solution is apparent when it is compared with the and detailed instructions with which every new introduced I think here again the analogy of drug doctor has been extended too far On the best way to drugs there is a certain measure of agreement though individual patients may react differently, but the best way to speak to patients there is not some agreement on the correct dose of digitalis f ten stone woman fibrillating at 120 beats per minute far less agreement on the correct type and dose of versation for a ten-years unhappily married vociferating at 120 words per minute Moreover there only three or four kinds of digitalis, but kinds of doctor, and even more kinds of women

No the prescribing of ourselves cannot be taught, partly instinctive, partly imitative, and partly by experience I do, however, consider it to be enormous importance and I propose to say some on the subject of conversation with patients

TALKING TO THE DOCTOR

Why does the patient want to talk to his doctor ?

First there is the natural desire for cc Many people simply want a pleasant chat, but going along to the local public-house for a drink of and a chat with the landlord they go along to the hospital for a drink of medicine and a chat with doctor The use of a doctor for this purpose is sary, and a pleasant gossip over a cup of tea with atients is equally satisfying Indeed one enlightened hysician tried the experiment of arranging outpatient ssions where the patients did not see the doctor at all less they specially asked for him †, this experiment as a great success. Moreover, despite the present high rice of tea, a cup of tea is cheaper than a bottle of edicine and far less likely to do any harm

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* From an address to the Medical Section of the British Psychological Society, forming a sequel to the chairman's by Dr Michael Balint published last week 83)

Another reason why people want to talk to doctors is get sympathy—they do not want help or advice they ant someone to know how much they are having to ear A vicar's wife told me once that much to his istress, parishioners were always wanting to show their lcerated legs to the vicar This was done not for spiritual ealing but that he might realise the extent of their ufferings It is a fact that it is easier to bear a heavy urden if that burden is visible to others. Doctors are old of all sorts of troubles—financial, domestic or ersonal—which are beyond their powers to relieve but ll the patient is seeking from them is some remark of the ind: I don t know how you put up with it all," or I think it s wonderful the way you manage to carry n ' Almost anything can be borne if someone thinks ne is wonderful

Some patients, unlike those I have just mentioned ome for advice They have problems which are soluble, nd they need, not sympathy, but a *suggestion as to* hat is to be done or not to be done Though it sounds aradoxical to say so I believe the advice given is often nmaterial The conversation helps the patient to make p his own mind, irrespective of the wisdom of the advice iven Only when he is strongly advised to do A does the verage person realise how much wiser it would be to o B

Other types of patient come not to see what the doctor as to say but already firmly decided on what he will say hey come, not for advice but to get medical backing or their own views. Whatever the doctor says they ill report that he confirmed their opinion If Mr ones says 'It s that terrible smell in the factory that s iven me this chronic stomach ' and the doctor says I m sorry to hear that ' he will be reported as saying The doctor said the fumes had poisoned my whole stem ' Or if Mrs Jones says Tommy got St Vitus ance because they caned him at school " and the doctor ays 'Hmmn she then reports this to her friends as The doctor said he d never seen such a terrible ase and his nerves ll never be the same after that aning '

In similar fashion those who wish to attribute illnesses tonsils air raids too much work at school damp alls, or being dropped as a baby will seek medical upport for their opinion Many of these people deserve ur sympathy and understanding Surely it is infinitely ore satisfying for them to rage at a bomb or to impugn tonsil than to try to accept that some illnesses have no ertain cause Fate is such an insubstantial target for lame compared with a damp wall a large tonsil or a ad smell

When a patient is seeking confirmation for an erroneous elief which does no-one any harm and gives him the omfort of something to blame it is questionable if much ood is done in correcting him but when he is out for ood, seeking ammunition with which to assail his nployers, his doctor or his hospital, then it is a very fferent matter This is an age of compensation not ly out of loyalty to our colleagues should we decline vitations from patients to criticise each other but for e good of the patients themselves The psychological rm done to patients by long-continued litigation is ten more extensive than the expense and trouble caused the medical profession

TALKING TO THE PATIENT

Having described some of the reasons why patients come to talk to doctors I now consider some of the ways a doctor can talk to his patients. As I have remarked, this is not a subject that can be taught, but it can be discussed, and I will consider it under various headings

First, *impressiveness* The impression a doctor makes *on his patient* is as important as the pharmacological action of the treatment he gives, but a doctor wishing to impress a patient must consider first whether he is *benefiting him* It is a good thing to give the patient confidence, but a doctor can pay more attention to the impression he is making on the patient than to the good he *is doing him* *Not only the way a doctor speaks* but his gestures, his manner and his smile all play their part There are also accessory aids—a book written by the doctor himself lying carelessly on the desk the use of a large shiny motor-car and chauffeur or (less expensive but quite effective) the skilful manipulation of a really thick pair of horn rimmed glasses Before using these adjuncts the doctor must consider whether he is trying to comfort himself or the patient It is a greater medical triumph to leave the patient feeling better but thinking little of the doctor than to leave him worse but deeply impressed

Secondly *tolerance* For a successful doctor patient relationship the doctor should try to achieve a level of tolerance and placidity nearing that of a saint He must be free of prejudice and not let the patient or his relatives irritate him Most of us have some foible, some little thing that rubs us up the wrong way I knew one children's doctor who could not bear mothers who overdid the word 'little" as in the sentence "He draws up his little legs, doctor and his little face is all screwed up when he passes his little motion I admit myself to an instinctive antipathy to patients who arrive for consultation chewing toffee or gum and also to patients who call me "Doc Such prejudices can and should be avoided The doctor's approach should not be 'Do I like this patient?" but 'Can I help this *patient?*" Experience will teach that many irritating mannerisms are caused by shyness and not by any desire to provoke for instance the patient who remains *apparently* buried in his newspaper when the doctor arrives at the end of his bed is rarely reading it he is probably assuming nonchalance because he is nervous.

Thirdly *lucidity* Misinterpretation of what the doctor says is so easy for the patient Many a doctor who has given an explanation on which he prides himself would be disconcerted to learn the retailed version of his carefully chosen words. One lady told me she had taken her boy to hospital where the doctor looked down his throat and told her the ear drum had grown right into the throat and was hanging out like a sausage He cut it off and said if he'd been five minutes later the child would have been dead I often wonder what he really said *I feel it cannot have been very clearly put*

Another example Last week a woman attending my hospital for her gastric ulcer assured me the house-physician had provided her with a new medicine which consisted of a strong solution of rubber dissolved in orangeade which was designed to fill up the cracks in the ulcer and set. This purpose she told me had been achieved

Both these patients were deluded but delighted but harmful *misinterpretation of doctors* remarks is even commoner That is why lucidity is so essential. It is a difficult art to cut one s explanatory coat according to the intellectual cloth provided by the *patient* and it must be especially hard for psychiatrists to word their interpretations without ambiguity because the is even harder to explain than the body

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† Bourne W A *Lancet* 1950 i, 127

Fourthly, *confidence* Confidence is an infectious thing—the doctor who possesses it is the doctor who can give it to others It must be sincere It is not much use pretending you are sure when you are not—the patient can tell Confidence is invaluable because if you are certain you are right and if you can convince the patient that you are right then whether you really are right or not often makes very little difference Yet the doctor should not assume omniscience I have a notion that doctors do not often enough say "I do not know" It is better to tell a man confidently that you don't know than to tell him unconvincingly that you do Patients can appreciate sincerity and truthfulness more than some people realise

Another quality that helps a doctor deal with people well is *unhurriedness* To give a patient the impression you could spare him an hour and yet to make him satisfied with five minutes is an invaluable gift, and of much more use than spending half an hour with him during every minute of which he is made to feel he is encroaching on your time I do not know if this special kind of unhurried placidity can be acquired purposely, but it is a most enviable faculty to possess

WHEN TO SPEAK

I now pass from the question of how to speak to the question of when to speak—in this case I mean when to probe beyond the purely physical side of a patient's illness Physicians see a large number of patients whose symptoms are purely physically caused and respond completely to physical treatment These require nothing except a prescription and a word of explanation Then there are patients whose symptoms, although organically caused, seem to be giving them more distress than is warranted by their severity Here it is well worth finding out what the patients' private beliefs about their symptoms are Fear of a more severe disease than the one affecting them is in my experience a common reason for so called functional symptoms Many a young woman may complain of mild aches and pains which by themselves hardly worry her enough to be noticed, but because she has known somebody crippled with rheumatoid arthritis these symptoms cause her profound anxiety which itself provokes the symptoms further Such women rarely mention their fear until it is sought out, but it is well worth seeking There is often a sigh of relief and magical disappearance of symptoms when the patient is reassured that her fears are groundless It is also just as common to find a man with unaccountable anxiety from minor symptoms because he has a fear of cancer Here again the dread of cancer is elicited only by tactful inquiries I think it is wise to ask all patients if they have any ideas about the cause of their symptoms and also to find out if they have any friend or relative suffering from a disease which they themselves fear Strangely enough, those who have a dread of a disease seem rarely to be the people who suffer from it, so the proportion of cures by reassurance in this group is high

Another type of patient where some probing may be rewarding is the hypochondriac—the patient who makes a hobby of doctors and drugs The woman who keeps a diary not of social functions but of pelvic functions, the woman who instead of taking up canasta takes up her bowels and who patronises the great colonic laundries of Harley Street If the doctor by his talk and his tact can interest her in the world outside instead of the intestines inside he will have achieved something really worthwhile

CONCLUSION

The truth about doctor-patient relationships is, I believe, almost impossible to ascertain We doctors know what our patients think of us and rarely learn what effect our talk, tact, and treatment have "He was so enthusiastic I didn't like to offend him commonly the attitude of the patient

Occasionally we get glimpses of the truth when overhear a conversation on top of a bus or when pati remarks are relayed to us by a friend (or more likely enemy), but in the main we remain ignorant, perhaps it is happier that we do so

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ESTIMATES FOR 1955-56

The National Health Service estimates[1] for 19 allow for an increase of £24,154,770 in net exp on the service (including Civil Defence services England, Wales, and Scotland Gross exper estimated at £537,888,365, compared with £511,73 in 1954–55, and appropriations-in aid at £74,518, compared with £72,522,350

The estimated gross expenditure is distributed follows

	£
Hospital, specialist and ancillary services	345,501
General medical, dental pharmaceutical, and supplementary ophthalmic services	149 471
Grants to local health authorities	23,506,
Training services, &c	1 686
Broadmoor Institution and State mental deficiency hospitals	1,682
Liabilities arising from the establishment of the service	5,10
Superannuation	8 006
Civil Defence services	1 [illegible]
Other services	705,
	£537,888,

The £345,501,315 estimated expenditure on the pital services is made up as follows advances to (capital account), £12,300,000, advances to (revenue account), £320,000,000, directly a hospitals, limb fitting centres, &c, £1,887,315, expenditure, £11,314,000

Estimated expenditure under most divisions shows an increase the largest is under advance boards (revenue account) where the increase is £20,5 Other increases include £2,312,000 for general me services (total £61,802,000) and £1,034,000 for dental services (total £27,537,000) The estimate Civil Defence services represents a reduction of £700 on expenditure in 1954–55

These estimates make no provision for the hos building programme announced earlier this year, e ture on which in England and Wales is expected amount to £7½ million in 1956–57, and to £10 in 1957–58[2]

Net expenditure by the Medical Research C in 1955–56 is estimated at £2,186,160, compared £1,974,869 in 1954–55—an increase of £211,291 the general expenses account estimated gross exp of £2,235,184 is made up as follows administ and central expenses, £95,292, National Institute Medical Research, £392,053, research units and ext scientific staff, £1,340,647, special grants to tions, &c, £184 242, temporary research grants training awards, £222,950 Under the building account, the cost of new building is shown as £84 and the cost of special apparatus as £16,100, a total of £100,100

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[1] Civil Estimates for the year ending March 31, 1956 Clas Health Housing and Local Government H M Stati Office 6s

[2] See *Lancet* Feb 19, 1955 p 410

Before Our Time

JAMES PARKINSON

Born April 11 1755

James Parkinson, whose *Essay on the Shaking Palsy* peared in 1817 was born in Hoxton lived all his life ere and was buried at the parish church of St Leonard's e term Parkinson's disease is now used throughout e medical world and the words ' Parkinsonism ' and Parkinsonian " have been added to the English nguage but Parkinson himself has been " forgotten the *English* and by the world at large "[1]

THE FAMILY

His father John Parkinson was a surgeon in practice Hoxton Square and he was the eldest of three children is sister Mary Sedgwick (born Jan 11 1763) married ohn Keys and his brother (born March 5 1761) died young man He married in St Leonard s Church, on ay 12, 1781 Mary Dale who is believed to have been e daughter of John Dale, a silk manufacturer who lived Charles Square Hoxton Six children were born of the arriage[2]

John Parkinson father of James, became a diplomate the Company of Surgeons soon after the surgeons parated from the Company of Barber Surgeons and 1775–76 he was anatomical warden under the master professor of anatomy He practised at no 1, Hoxton quare for many years until his death A memorial one is still visible affixed to the wall of the verger's ouse in the precincts of St Leonard's Church Shore itch and the inscription John Parkinson, surgeon te of this parish died 10th January 1784, aged 50, ' is ill readable though the epitaph below is undecipherable No 1 Hoxton Square is a corner house on the south est corner of the square and it was still standing in 1910 It had three storeys and a basement with a two-storeyed uilding behind it having an entrance on to the side street, nd behind this a single-storeyed room that might have rved as a shop[1] Nothing exists today except the old front llings the house was demolished many years ago and a ctory now occupies the site Parkinson in his will refers to e contents of his shop and it is probable that he kept an en shop for the sale of medicines, which would enable him charge for those he dispensed himself The house was never ned by the family though they had occupied it for so many ars the owner being a Joshua Jenning The whole of the quare which was built in the middle of the 18th century as owned at one time by Israel Wilkes father of the notorious ohn Wilkes.

Charles Square and Hoxton Square were the two best sidential areas in Hoxton and the Parkinson family had as eighbours the vicar of St. Leonard s Church, another surgeon, wyers tradesmen and several distinguished Nonconformist ivines Today the only residents are the vicar of St Leonard s hurch and the clergy of St Monica s Roman Catholic Church. early all the other buildings are furniture factories. Some of the buildings were destroyed in air-raids but the ancient trees in the centre still flourish and the garden is well kept Two other buildings in the square in Parkinson s time were the Hoxton Square Coffee House and a Nonconformist meeting house

MEDICAL WRITINGS

James Parkinson had an urge to write and as an apprentice he boldly challenged theories of Dr Hugh Smith the younger who had published a book entitled *Philosophy of Physic* and another entitled *Philosophical Inquiries* in 1780 A tract on these books though published anonymously, is attributed to Parkinson

His father was medical assistant to the Royal Humane Society for the New River area, which meant that he was on call for cases of drowning A report of the society for 1778 records that an honorary medal was presented to James " for the recovery of the body of Brian Maxey," on Oct 28 1777

The report of the case which was written by John Parkinson the father states that he and his son were called to a house in Hoxton where a man had hanged himself When they arrived at the house they found him pulseless and to all outward appearances dead but after carrying out the restorative methods recommended by the society—e g., inflation and deflation of the lungs friction, &c —the pulse returned in half an hour natural breathing in forty minutes, and in ninety minutes his senses returned. The patient expressed his sorrow for his horrid crime and the greatest gratitude to those who were instrumental in his restoration to his wife and children."

Parkinson was in good company for Dr Hawes and Dr Cogan instigators of the Royal Humane Society and the illustrious Dr J C Lettsom were medical assistants for the Thames between London Bridge and Westminster Bridge

The society paid two guineas to those attempting resuscitation for two hours, a guinea to the landlord of the public house used as a receiving house and half a crown to the messenger A further two guineas was awarded to the medical assistant if the patient recovered As most of the medical assistants refused payment medals were awarded to them instead. The medal which was silver and had the recipient s name engraved on it was bequeathed in Parkinson s will to his medical son.

Parkinson had had a sound liberal education at a time when most surgeons are said to have been ill-educated He had an extensive practice, and he early showed that he was a keen observer with unusual clinical acumen He wrote many articles for medical journals on cases which he met in his practice as well as those he had been called to see as a medical assistant of the Royal Humane Society

He described the treatment of a child aged 14 months who was found lying face downwards in a tub of water; the attempted resuscitation of a youth who had been drowned and his experiments with an electrical apparatus on the muscles of the limbs the treatment of a servant girl of 28 who was suffering from hydrophobia, and who afterwards died in the London Hospital the treatment of two men who were struck by lightning in a house in Shoreditch both of whom recovered and the recovery of a farm labourer who had been blinded by a flash of lightning while driving cattle in from a field on a stormy night He described a case of trismus, following a compound fracture of the bones of the leg, in which the patient recovered after treatment with heroic doses of tincture of opium and drastic purgation. In a report in 1812 on the post-mortem examination of a boy of 5 he describes a *perforated gangrenous appendix with peritonitis*, believed to be the earliest reference to the disease in English medical literature[3]

He also wrote popular books Today they would have some such titles as ' Home Doctor ' or First Aid for the Sick and Injured. But at the turn of the 18th century they were called *Medical Admonitions for Families* (1799) and the *Villager s Friend and Physic* (1800) A first aid sheet intended to be hung cottager's fireside was called *The Way to H* He wrote a book for children *Dan* which pointed out the dangers of rough games.

Rowntree L. G *Bull Johns Hopk Hosp* 1912 23 33

The first child, James John (born Feb 11 1783) died in infancy the second, John William Keys (born July 11 1785) was apprenticed to his father and became a surgeon the third was Emma Rook (born April [illegible] 1788) the fourth Jane Dale (born Oct 2 1789) died Jan. [illegible] 1792 the fifth Henry Williams was born May 7 1791 and the sixth Mary Dale, was born March 8 1794 James his brother and sister and all his six children, were baptised in St. Leonard s Church.

John William Keys Parkinson married Diana Chapple in St Leonard s Church, on May 7 1811 and they had two children, James Keys (born Oct 29, 1812) and Mary Hester (born March 30 1816) After his wife's death he married again and his wife, Elizabeth Caroline bore him a son, John Ellis (born July [illegible] 18[illegible]0)

Emma Rook Parkinson married John Dymock of Stonehouse Gloucestershire on Oct. 29 1816 at St Leonard s Church, and they had four children The eldest Emma Parkinson Watts Keys Dymock (born November 1821 died Aug 28 1867) married Edward Brown of Croydon The youngest, the Rev Nathaniel Dymock M.A Oxfd, died in 1900, aged [illegible], having been rector of Wymonsfold, Kent and vicar of St Paul s Church Maidstone The other two children died in their teens.

Henry Williams Parkinson married Elizabeth Ascott and left the country to live in Calcutta Mary Dale Parkinson was unmarried at the time of her father's death.

It is probable that descendants of John Watts Keys Parkinson and Emily Rook Dymock are living today

3 Shepherd J A *Lan*

Parkinson suffered from gout, as did his father before him, and in his *Observations on the Nature and Cure of Gout* (1805) he described in detail their symptoms and his own theory as to the origin and pathology of gout But despite the painful enlargements of the interphalangeal joints of his right index finger, he wrote a bold unwavering hand, as may be seen by one of his letters dated 1812, which is in my possession

In his tract, *Hints for the Improvement of Trusses* (1802), which sold for only a few pence, he pointed out the danger of strangulation and how necessary it was for those doing heavy labour to wear a truss A plate was included showing the stages in the construction of the appliance which he had designed for the control of inguinal hernia, which could be constructed by any handy man at a small expense In the preface he deplored the fact that a surgical appliance—a necessity for the preservation of life—could be patented and thus become "a species of monopoly."

Outside his profession he had many interests His *Chemical Pocket Book* (1799) reached five editions His main interest and hobby, however, was geology He had a collecting instinct which grew with the years, and he collected fossils His monumental work on palæontology, *Organic Remains of a Former World* (1804–11), consisted of three large volumes with plates engraved from drawings which he himself had made The cost of these volumes was ten guineas, a large sum in those days, but it must have sold well because there are over twenty copies of it in London libraries alone This work was reprinted twenty six years after his death by his friend, Dr Gideon Mantell, another medical man who became a celebrated geologist

POLITICAL ADVENTURES

Parkinson lived during the French Revolution and the long war with France He was a pacifist and a political reformer, and he wrote many pamphlets under the pseudonym "Old Hubert," in which he advocated the reform of representation of the people in the House of Commons, the institution of annual Parliaments, and universal suffrage He became a prominent member of the London Corresponding Society and the Society for Constitutional Information which had these reforms as their aims

In 1794 the leaders of the societies were arrested and tried for high treason, but were acquitted Parkinson was subpœnaed as a witness at the trial of Thomas Hardy, the founder of the London Corresponding Society, but was not called to give evidence

Shortly before the trials of the leaders, three members of the London Corresponding Society, well known to Parkinson, were arrested and imprisoned without trial, the Government having suspended the Habeas Corpus Act in order to do this They were accused of plotting the assassination of King George III by means of a poisoned dart The deed was to be perpetrated from the pit of the theatre while the King was sitting in his box Parkinson, convinced of the innocence of the accused, wrote to the Privy Council offering to give evidence to prove their innocence The offer was accepted, and in his pamphlet *Assassination of the King* Parkinson set out from memory the questions he was asked and his replies The supposed plot was a frame up, based on false evidence concocted by a Government informer who had been a member of the society, and the prisoners were later freed

The Privy Council were astonished when Parkinson revealed that he was the author of a pamphlet *Revolution without Bloodshed* (1794) His other pamphlets were bitter, sometimes venomous satires, though often mixed with touching pathos One, in particular, was addressed to Edmund Burke In his *Reflections on the French Revolution* Burke referred to the common people as "the swinish multitude" Some 40 tracts were published in reply, including one by Parkinson, *An address to the Hon Edmund Burke from the Swinish Multitude* (1[illegible] in which he wrote

"As to yourself, good sir, there are those who c resemble the venomous asp, whose poison is placed its tongue, or the Camelon, and like that creature, appearance ever changes with your situation"

SOCIAL REFORMS

The wretchedness of the labouring poor, the and misery of their homes in Hoxton and had made Parkinson an ardent social reformer He had an unfortunate experience

He was called to see a widow named Mary D Rosoman Street, Clerkenwell, who had been wandering the street at night, had heard voices coming down the accusing her of having killed her husband, and who concealed a knife in her dress, presumably with suicidal Parkinson saw her after she had been admitted to a asylum As a result of his examination he did not think she was certifiable, so he made inquiries in neigh houses, questioned her nephew and niece Mr and Benjamin Elliott, her lodger, and her son aged 16, who he was convinced that his mother was insane returned to the mad house, and, as a result of a examination, signed the certificate for her detention.

After a few weeks she was sitting looking out of the when she saw a woman friend, to whom she shouted that was being detained against her will The friend inf brother, and other friends, who secured her release years later, Benjamin Elliott was tried at the C sessions house, on an indictment charging him, his wife, Sarah Bodkin, with conspiring to deprive Mary D of her liberty He was found guilty and sentenced months' imprisonment

A storm of criticism of Parkinson's conduct appeared daily press He was accused of certifying Mary Daintree as the result of his own observations, but on info supplied by others Fellows of the Royal College of Phys who were visitors in lunacy, expressed surprise that he not "contradicted the calumnies raised against him" son, now aged 19, in the witness box denied that Par had ever questioned him, and Parkinson did not recognise though he did afterwards, when it was too late

In a tract, entitled *Mad-houses Observations on Act regulating mad houses* (1811) he vindicated h and suggested that two medical certificates ought to required, instead of one, and that the aid and di of a justice of the peace was necessary

In 1819 Parkinson published a tract *Observations necessity for Parochial Fever Wards* He related h an epidemic of fever among the inhabitants of one of numerous courts off the Kingsland Road, Shoreditch, could not obtain the services of hired nurses and bours shunned them He suggested that parochial wards should be established, containing 18 beds (6 men, and 12 for women) for a population of say persons When the epidemic was over the building be used as an infirmary Parkinson was visiting p to the parish infirmary in the Kingsland Road, which built in 1777, and St Leonard's Hospital now stan the site He deplored the fact that there was only hospital for pauper fever patients in London, and th 70 beds were inadequate It was over fifty years an Act forced local authorities to provide iso accommodation for fever cases

Fully occupied as he must have been with his m practice, and despite his devotion of his leisure h his favourite science, he found time to interest in the affairs of the parish of St Leonard In 1 was elected by his fellow-parishioners a trustee for liberty of Hoxton, and he remained a member of the until he died

The committee which managed the Sunday school at St Leonard's Church, appointed him as secretary 1807, Mr Samuel Whitbread, M P, the brewer, b Bill before the House of Commons to establish in every parish throughout the country, for the of poor children, whereby each child should have opportunity of attending school for two years at expense of the State Parkinson wrote a tract *C* ns on *Mr Whitbread's Plan for the Education of the bor* (1807), in which he said that a debt of gratitude was e to the proposer of the Bill, but he feared that as a sult of the establishment of these parochial day schools e Sunday schools would suffer He maintained "that mere literary education without the inculcation of oral and religious principles would prove highly *jurious.*" *Furthermore* the parents whose children rned one to three shillings per week up to the age of 14 d five shillings per week after this age, were unlikely to rego this money for the sake of the children s education. Much concerned with the welfare of the children of the unday school, he kept a register containing the names all children who were seeking employment, with rticulars concerning their abilities, behaviour &c., hich was open to inspection by prospective employers, cause he felt that the welfare of poor children was eatly influenced by their first situations in employment He was also concerned for the welfare of pauper ildren of the parish who were apprenticed to masters d mistresses not in their own parish, but in neigh uring parishes, lest they should become chargeable in ult life He reflected that no law existed by which the ities of the employer were defined, nor were any spectors appointed to visit the children to see the nditions under which they worked. He succeeded in rsuading the vestry to appoint some of the trustees voluntary visitors. Later, visitation by paid inspectors as laid down by Act of Parliament.

About this time Malthus maintained that the earth ould not be able to yield enough food to feed the pidly increasing population Parkinson thought other se and said that if the population exceeded the means support the fault lay not in nature but in the ability politicians to discover some latent defect in the laws specting the division and appropriation of property'

PARKINSON'S DISEASE

In 1817 he wrote the *Essay on the Shaking Palsy* hich has brought him posthumous fame in the medical orld His description of the disease which now bears s name has never been bettered, though it has been panded He considered the cause to be principally n the medulla spinalis of the cervical region its mem anes, or the containing theca' and he hoped that some ctor would one day have the opportunity of examining e body of a patient who had died from the disease— r he modestly apologised for the hypothetical nature his observations on its pathology The following tract from the essay is an example of his pleasing erary style

> "The patient experiences much inconvenience, which *happily is found daily to increase* The submission of the mbs to the direction of the will can hardly ever be obtained in e performance of the most ordinary offices of life The gers cannot be disposed of in the proposed directions, and plied with certainty to any proposed point. As time and e disease proceed difficulties increase writing can now be rdly at all accomplished and reading from the tremulous ption, is accomplished with some difficulty Whilst at meals e fork, not being duly directed, frequently fails to raise the orsel from the plate which when seized is with much fficulty conveyed to the mouth. At this period the patient ldom experiences a suspension of the agitation of the limbs. mmencing for instance in one arm, the wearisome agitation borne until beyond sufferance, when, by suddenly changing e posture it is for a time stopped in that limb to commence nerally in less than a minute in one of the legs, or in the n of the other side Harassed by this tormenting round patient has *recourse to walking a mode of exercise* to hich the sufferers from this malady are in general partial; ing to their attention being thereby somewhat diverted m their unpleasant feelings, by the care and exertion uired to ensure its safe performance'

LAST YEARS

It has been said that Parkinson received no honour recognising the disease as a clinical entity, nor for his work on palæontology True he was given no honorary degree nor was he elected to the fellowship of the Royal Society, but he did receive recognition from the Royal College of Surgeons of England, whose honorary gold medal was awarded him in 1822 He was indeed, the first to receive this award (instituted twenty years before) and it has been bestowed only fifteen times in the past hundred and fifty years, the recipients including Lord Lister Sir James Paget and Richard Owen

It seems clear, too that Parkinson was held in high esteem by his fellow general practitioners, for in 1818 he was chairman of the Association of Apothecaries and Surgeon Apothecaries of England and Wales He was also a member of many learned medical and geological societies He was one of eleven people who met at the Freemason's Tavern, Great Queen Street, in 1807, and founded the Geological Society of London, and he was on the council from 1813 to 1815 He was a member of the Wernerian Society of Edinburgh and the Cæsarean Society of Moscow He was a fellow of the Medical Society of London, and a member of the London Medical and Chirurgical Society

Parkinson is believed to have retired when he exchanged houses with his son, who continued the family practice in Hoxton Square He died on Dec. 21, 1824 at no 3, Pleasant Row, Hoxton and an entry in the burials register of St Leonard's Church reads: 'No 741 James Parkinson, Kingsland Road buried December 29th 1824 R Crosby" His remains were interred in the graveyard attached to the church, but no tombstone can now be found

No portrait of Parkinson is known to exist, and the only description we have of him is by his friend Mantell who wrote 'Mr Parkinson was rather below middle stature with an energetic intelligent, and pleasing expression of countenance, and of mild and courteous manners readily imparting information either on his favourite science or on professional subjects"

Parkinson was truly a general medical practitioner; and his impact on his own generation and his influence on succeeding generations is shown by the number of his ideas, both social and scientific, that are now generally accepted.

My thanks are due to Dr W McMenemey Dr J Dymock, and Mr Jackson borough librarian at Shoreditch for their assistance in obtaining biographical details

A. D Morris
M.D Brux., M.B Lond.

Points of View

HOLES, KNOBS, AND WIRES

Abstract Art and Auto-suggestion

Sir Henry Turner, C.B.E.

The public is in these days learning in some degree to tolerate persons who act abnormally We try to persuade ourselves that they are sometimes, in effect being pushed from behind and not just "bloody minded' And I think that we ought to use this charitable approach in considering why artists—many of them possessing unquestionably skilful technique—produce what are at *first sight* (and often later) meaningless doodles lumps of stone pierced by quite unsuggestive holes, tangles of wire and so forth

So, with a layman s proper timidity I shall attempt an answer to the questions—'Why is abstract art produced, and why is it taken seriously by people seemingly well qualified to appraise it?'

* * *

In the first place I would suggest this experiment Take three (or more) upholsterer s coiled springs, entangle them and mount the result in an inverted aquarium bowl indirectly lit with a professionally lettered card reading (for example) *Time Passing* This should be exhibited in a place of some importance Failing the Tate, *a Bond street art-dealer's window will do*

The reactions of observers will fall into four categories

(a) Confident, extravert derision

(b) Open disconcertment "I suppose I ought to see something in it"

(c) Insincere praise, to dodge a charge of artistic insensitivity

(d) Prolonged study, and a true statement of pleasure in a new æsthetic experience

There is no reason to trouble about (a) They are happy enough, even though scorned by the others But something can, I think, be done about the uncomfortable inferiority feeling of (b), and the unpleasant, self damaging deceitfulness of (c) The remedy seems to lie in an understanding of the auto hypnotic process employed by class (d), who are the prime instigators of the confusion

The proposition which I would like considered by better qualified readers is that the key to understanding both the origin and the appreciation of abstract art lies in the mechanism of auto hypnosis By this mechanism the observer persuades himself that the object possesses in itself a quality affording æsthetic pleasure

In the experiment I have recommended, all the apparatus is present for producing, first, a light hypnoidal state, and, second, a post hypnotic effect There is the steady gaze, the illumination casting surrounding objects into relative gloom, respect, tinged perhaps with awe, for the creator of the intriguing Thing, a pretty strong initial conviction that the Thing has profound significance, and not merely a hope, but an expectation of satisfaction through artistic achievement The effect of all this, upon a hypnotically susceptible person, is to turn on, so to speak, the switch marked Æsthetic Thrill

From this it seems to follow that literally *any* object can be used as an emotional trigger by class (d), supposing the right circumstances They self-induce emotion, and then use that emotion as proof that something tangible exists as its rational cause The people who can perform this pleasurable mental antic could equally well, presumably, produce religious exaltation, quickened body-healing power, and all the other phenomena which result from successful auto- (or hetero-) suggestion It would be interesting to know whether all those who can achieve admiration for abstract art are in fact "good" subjects for post-hypnotic suggestion in general

My hypothesis gains some corroboration from the fact that the phases of successive cults of purely abstract art are briefer than those depending on more direct appeal—i e, the straight, representational, associative styles The relatively short lives of Dadaism and Cubism may be due to their dependence on auto hypnosis Hypnotic suggestions do, I believe, tend to wear out, they wear out too soon for them to be widely transmitted, by training, from one generation to another Surrealism seems to be lasting better, because it uses recognisable objects which, although irrationally juxtaposed, do provide some ordinary associative prompting

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Public Health

COWPOX IN MAN

And its Relationship with Milker's Nodule

BERNARD LAURANCE
M B Lond, M R C P, D C H

*CONSULTANT PÆDIATRICIAN, DERBY CITY HOSPITAL
DERBYSHIRE HOSPITAL FOR SICK CHILDREN, LATELY
REGISTRAR, BRISTOL ROYAL HOSPITAL FOR SICK*

PROPHYLACTIC inoculation against smallpox with fluid from a vesicle or pustule of a patient the disease is known to have been practised for centuries in various parts of the world In ancient dried crusts from a smallpox pustule were inserted the nostril on "a lucky day"—a practice known "sowing the smallpox" This is a fine example of successful empiricism of some ancient Chinese for we now know that variola virus can survive for a year in dried crusts and floor dust (Downie and D 1947)

Variolation was introduced into England at the of the 17th century Before then many travellers brought back news of this form of inoculation, Dr Martin Lister was probably the first to cc the method to the medical profession in this In 1695 he published a tract on smallpox that in correspondence between the secretary of the R Society and many physicians from abroad possibly led to the famous letter written in 1713, read by Dr John Woodward to the society in 1714 which Dr Timoni of Constantinople advocated the duction of inoculation into Great Britain (Stearns There is some evidence that the method was before this time in South Wales (Shrewsbury 1951)

For the adoption of the practice in this Lady Mary Wortley Montagu, the wife of the Ambassador to the Ottoman Court, was responsible She was impressed by the methods she seen practised in Turkey to lessen the dreaded of smallpox, and wrote to her friends in England of experiences The following is an extract from a written in 1717

> "Apropos of distempers, I am going to tell you a that I am sure will make you wish yourself here The so fatal, and so general amongst us, is here entirely by the invention of *ingrafting*, which is the term they give There is a set of old women who make it their business perform the operation every autumn, in the month of ember, when the great heat is abated People send to another to know if any of their family has a mind to have smallpox, they make parties for this purpose, and when are met (commonly fifteen or sixteen together), the woman comes with a nutshell full of the matter of the sort of smallpox, and asks what veins you please to opened She immediately rips open that you offer to her a large needle (which gives you no more pain than a scratch) and puts into the vein as much venom as can upon the head of her needle, and after binds up the little with a hollow bit of shell, and in this manner opens f five veins The French Ambassador says pleasantly, they take the smallpox here by way of diversion, as they the waters in other countries"

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It is appropriate that the following description of a all outbreak of cowpox should come from a part of oucestershire only seventeen miles from Berkeley nner's home in Gloucestershire

Clinical Account

The outbreak took place on a small farm some five miles m Bristol. A herd of eighteen cows, to which there had been no recent addition was kept About Dec. 1 1953 the farmer noticed that some of the herd were generally upset and irritable and that at milking time they kicked more than usual. Their yield of milk diminished for about ten days and hand milking which was practised became even more difficult when the teats swelled and vesicles appeared on their surface (fig 1) These vesicles later ulcerated (fig 2) producing an obnoxious smell that only a Gloucestershire farmer's colourful dialect could describe In his second book—*Further observations on Variolæ Vaccinæ* (1799)—Jenner mentions a doctor friend's report that the cows ' gave off an offensive stench from their udders, though he considered this odour unusual among cows affected by cowpox

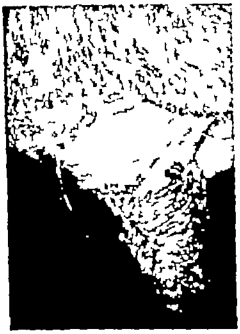
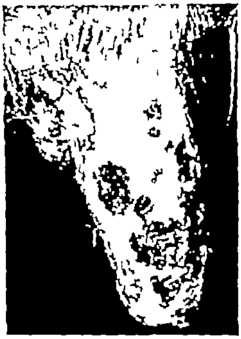


Fig. 1—Vesicles on cow's teat.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On Dec 3 the farmer aged 32 and never vaccinated previously noticed a pimple on the dorsum of his right thumb subsequently it became a vesicle and scabbed over one week later (fig 3) During this week a pimple also appeared on the right index finger but rapidly disappeared At the same time there was headache lassitude fever and lymphangitis with axillary and epitrochlear lymphadenitis of the right arm. He had to work throughout this illness, and on Dec 19 he felt worse and the scab on the thumb was larger (fig 4) Two days later the scab separated together with some pus which had probably formed as the result of secondary infection. He then recovered and the thumb healed leaving a small scar

The only other persons living on the farm were the farmer's wife his daughter and a cowman all of whom had been vaccinated in infancy and were unaffected by the cowpox No other outbreak was reported in either cows or man in the neighbourhood

Virology

Dr J A Dudgeon of St. George's Hospital Medical School kindly investigated serum from the farmer which was taken on the ninth and eighteenth days of the disease Unfortunately no vesicle fluid could be obtained for the lesion had scabbed over by the time it was first seen There was a distinct rise in complement fixing antibody to the viruses of both vaccinia and cowpox

Specimen of serum	*Cowpox virus*	*Vaccinia virus*
9th day of disease	1 : 10	1 : 5
18th day of disease	1 : 160	1 : 320

These viruses are generally held in this country to be distinct though closely related the virus of vaccinia being a laboratory strain the precise origin of which is not clear

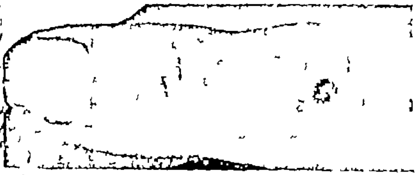
Fig 3—Farmer's thumb one week after appearance of vesicle.

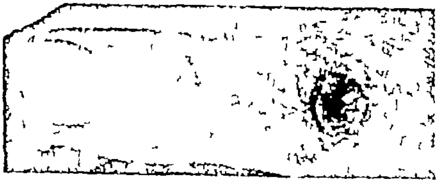
Fig 4—Farmer's thumb about fifteen days after appearance of vesicle

lettered card reading (for example) *Time Passing* This should be exhibited in a place of some importance Failing the Tate, a Bond street art dealer's window will do

The reactions of observers will fall into four categories

(*a*) Confident, extravert derision

(*b*) Open disconcertment "I suppose I ought to see something in it"

(*c*) Insincere praise, to dodge a charge of artistic insensitivity

(*d*) Prolonged study, and a true statement of pleasure in a new æsthetic experience

There is no reason to trouble about (*a*) They are happy enough, even though scorned by the others But something can, I think, be done about the uncomfortable inferiority feeling of (*b*), and the unpleasant, self-damaging deceitfulness of (*c*) The remedy seems to lie in an understanding of the auto hypnotic process employed by class (*d*), who are the prime instigators of the confusion

The proposition which I would like considered by better qualified readers is that the key to understanding both the origin and the appreciation of abstract art lies in the mechanism of auto-hypnosis By this mechanism the observer persuades himself that the object possesses in itself a quality affording æsthetic pleasure

In the experiment I have recommended, all the apparatus is present for producing, first, a light hypnoidal state, and, second, a post hypnotic effect There is the steady gaze, the illumination casting surrounding objects into relative gloom, respect, tinged perhaps with awe, for the creator of the intriguing Thing, a pretty strong initial conviction that the Thing has profound significance, and not merely a hope, but an expectation of satisfaction through artistic achievement The effect of all this, upon a hypnotically susceptible person, is to turn on, so to speak, the switch marked Æsthetic Thrill

From this it seems to follow that literally *any* object can be used as an emotional trigger by class (*d*), supposing the right circumstances They self induce emotion, and then use that emotion as proof that something tangible exists as its rational cause The people who can perform this pleasurable mental antic could equally well, presumably, produce religious exaltation, quickened body-healing power, and all the other phenomena which result from successful auto- (or hetero-) suggestion It would be interesting to know whether all those who can achieve admiration for abstract art are in fact "good" subjects for post hypnotic suggestion in general

My hypothesis gains some corroboration from the fact that the phases of successive cults of purely abstract art are briefer than those depending on more direct appeal—i e, the straight, representational, associative styles The relatively short lives of Dadaism and Cubism may be due to their dependence on auto hypnosis Hypnotic suggestions do, I believe, tend to wear out, they wear out too soon for them to be widely transmitted, by training, from one generation to another Surrealism seems to be lasting better, because it uses recognisable objects which, although irrationally juxtaposed, do provide some ordinary associative prompting

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Public Health

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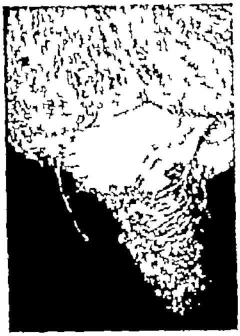
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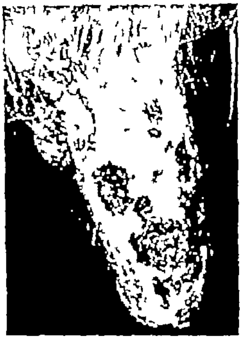
Fig 2—Ulcers on cow's teat.

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The only other persons living on the farm were the farmer's wife, his daughter and a cowman, all of whom had been vaccinated in infancy and were unaffected by the cowpox No other outbreak was reported in either cows or man in the neighbourhood

Virology

Dr J A. Dudgeon of St George's Hospital Medical School kindly investigated serum from the farmer which was taken on the ninth and eighteenth days of the disease Unfortunately no vesicle fluid could be obtained for the lesion had scabbed over by the time it was first seen. There was a distinct rise in complement fixing antibody to the viruses of both vaccinia and cowpox:

Specimen of serum	*Cowpox virus*	*Vaccinia virus*
9th day of disease	1:10	1:5
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These viruses are generally held in this country to be distinct though closely related the virus of vaccinia being a laboratory strain the precise origin of which is not clear

Fig 3—Farmer's thumb one week after appearance of vesicle.

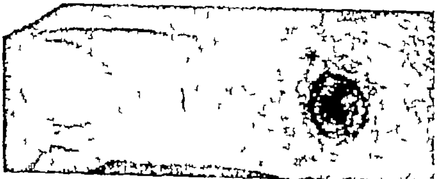
Fig. 4—Farmer's thumb about fifteen days after

Discussion

Recent medical literature includes few references to cowpox in man Possibly the disease is thought not worth recording, particularly in view of adequate earlier accounts, certainly it became less common after the introduction of vaccination, but with the declining popularity of vaccination it may be seen more often According to local veterinary practitioners the disease is still fairly common among cows in the West Country, but is rare in horses

Most veterinary authorities distinguish vaccinia of cows from cowpox of cows Cow vaccinia originates in man, whereas cowpox is a specific disease of cows, independent of infection from human sources, though giving rise to cowpox in man (Davies et al 1938) Nomland and McKee (1952), however, consider that genuine cowpox in cows arises from contact with recently vaccinated persons Cows are usually ill, and their yield of milk decreases, when they have cowpox, they recover in a few weeks When human beings contract the disease from cows, they develop headache, malaise, and fever, and lesions typical of vaccinia appear

Such a description accords well with the outbreak reported here, though no recently vaccinated person is known to have been in contact with the cows for a considerable time before the outbreak The rise of antibody titres to both cowpox and vaccinia confirms the diagnosis of cowpox in the farmer

Cowpox in man needs to be distinguished from "milkers' nodules"

Bonnevie (1937) gives an account of "milkers' nodules," which he terms "milkers' warts," ascribing this disorder to a virus allied to that of vaccinia Characteristically, nodular lesions appear on the teats of the cattle, but do not upset them constitutionally The nodules give rise to painless, bluish red, indolent nodes on the hands, arms, and face of milkers Usually there are no constitutional symptoms, though axillary adenitis is sometimes present The incubation period is eight to ten days, and the lesions heal after six to ten weeks, without scarring, unless there has been secondary infection Vaccination against smallpox does not prevent the nodules from appearing (Davies et al 1938, Danbolt 1949, Nomland and McKee 1952)

Clinically, genuine cowpox or vaccinia is easily distinguished from false cowpox or milkers' nodules. The cowpox virus was identified many years ago, but that of milkers' nodules has eluded many investigators The evidence seems to point to its being allied to, but distinct from, the cowpox virus, the infection has often been termed paravaccinia of Lipschutz (Morozov 1940, Becker 1940) Lately, Findlay and Haig (1952) claim to have isolated the virus

In Jenner's original monograph the two conditions were clearly distinguished, for he wrote

> "It is necessary to observe that pustulous sores frequently appear spontaneously on the nipples of Cows, and instances have occurred, though very rarely, of the hands of servants employed in milking being affected with sores in consequence, and even of their feeling an indisposition from absorption
>
> "These pustules are of a much milder nature than those which arise from that contagion which constitutes the true Cow Pox They are always free from the bluish or livid tint so conspicuous in the pustules in that disease No erysipelas attends them, nor do they shew any phagedenic disposition as in the other case, but quickly terminate in a scab without creating any apparent disorder in the cow This complaint appears at various seasons of the year, but most commonly in the Spring, when the Cows are first taken from their winter food and fed with grass It is very apt to appear also when they are suckling their young
>
> "But this disease is not to be considered as similar in any respect to that of which I am treating (i e, cowpox), as it is incapable of producing any specific effects on the human constitution
>
> "However, it is of the greatest consequence to point it ore, lest the want of discrimination should occasion an idea of security from the infection of the smallpox, might prove delusive"

I wish to thank Dr E P K. Rushton, of P Gloucestershire, for informing me about the farmer in instance Prof F Blakemore, of the University of B kindly gave me help on the veterinary aspects of this The photographs were taken by the department of photography, University of Bristol

REFERENCES

Becker, F T (1940) *J Amer med Ass* **115**, 2140
Bonnevie, P (1937) *Brit J Derm* **49**, 165
Danbolt, N (1949) *Tidsskr norske Lægeforen* **69**, 177
Davies, J H T, Janes, L R., Downie, A. W (1938) *Lanc* 1534
Downie, A W, Dumbell, K R (1947) *Ibid*, i, 550
Findlay, D H, Haig, D A (1952) *Brit J Derm* **64**, 453
Hagan, W A., Bruner D W (1951) Infectious Diseases of Dom Animals London, p 697
Jenner, E (1798) An Inquiry into the Causes and Effects of Variolæ Vaccinæ London
Montagu Lady M W (1717) Cited by L Clendening (1 Source Book of Medical History New York, p 293
Morozov, F N (1940) *J Microbiol Moscou*, **8**, 25
Nomland, R, McKee, A P (1952) *Arch Derm. Syph*, Chic **65**, 663
Shrewsbury, J F D (1951) *Queen's med Mag* **44**, 24
Stearns, R. P (1950) *Bull Hist Med* **24**, 103

Medicine and the Law

The Overturned Inhaler

A 9-year old girl was under treatment in a childre hospital following poliomyelitis, she could not move legs, had to be propped up to sit, and had only a limi use of fingers and arms When she developed s bronchial trouble, the nursing staff, after various exp ments, devised a method of enabling her to use an inha herself they propped her up in bed, put a pillow her lap, and placed the padded inhaler bottle in a d tray on the pillow The child was then able to put hands round the inhaler and reach the spout At f she did it with someone standing over her, but later managed it herself while the nurse in the ward went with other duties This worked successfully for months

At 6 30 one morning the night nurse, who had sixt children and two wards to attend to, woke the child gave her the inhaler in the usual way The nurse then to go to the sluice about ten paces down the corri While she was out of the ward, she heard cries and c back to find that the inhaler had somehow been ti over and its scalding contents had soaked throug the child's legs and thighs, causing second-degree bu The child by her mother brought an action for neglige against the group hospital management committ Mr Justice McNair held that neither the nurse nor administration had been negligent The plaintiff appeal

In the Court of Appeal on March 28 Lord Jus Denning said that the court agreed with the judge t the positioning of the child and the inhaler were best that could be devised, and that the defendants w not negligent on that point The more difficult quest was whether this little girl, helpless as she was, ought have been left alone at all while using an inhaler c taining boiling water To answer it the court had consider the situation both of the nurse and of the hosp system

The nurse was dealing with the other little g She had to be near at hand in case of difficulty, and had been near at hand all the time in the very wa except for the few moments or seconds when she went the sluice Was that negligence on her part to leave room for that very short while? It might have be negligence in the early stages before it had been se that the little girl could manage the inhaler But t judge was right in holding that, after she had managed quite well for two months, it could not be negligence the part of the nurse, who had all these children un her care, to leave the ward for that very short time

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[1] See *Lancet*, 1954 ii, 1332

Vas the administration then to blame for not having anged for the inhalations to be done at a time when the se was not so rushed, or for not telling her that if she s called out of the room she should put the tray le? The court could not consider those matters, for y had not been investigated before the judge One l to be careful in these cases not to be wise after the nt. Hospitals and nurses had the whole round of ly duties to attend to, and, with all the skill and care at could reasonably be expected of them, misadventures l occur This was such a misadventure, as the judge d found, though it was one which might perhaps help prevent others in future

Lord Justice Parker and Mr Justice Roxburgh agreed d the appeal was dismissed.

Alleged Libel by Doctor

A man sued a limited company for damages for rsonal injuries sustained in a road accident, and the mpany's solicitors instructed a doctor to examine him fter doing so, the doctor made a report to the solicitors ho quoted part of it in a letter to the patient's solicitors s follows:

> I then asked him what he would do if I recommended im to go back to work at once; he replied that he would o but that he would need three secretaries a chauffeur and ndry other bodies to do the work he formerly carried out ingle-handed because he would be unable to do the work imself I then asked him how long he thought it would be efore he recovered and he stated that he could wait 50 or 60 ears if necessary
>
> His demeanour during this interview was almost a cari ature—lying in bed smoking a cigar in his private single oom the picture of comfort with his radio and photographs. e was cocksure arrogant and self-opinionated

The patient saw this letter and started proceedings gainst the doctor for damages for alleged libel. The octor in his defence claimed inter alia that the eport was privileged The plaintiff in reply alleged nalice.

Mr Justice Donovan on an application by the laintiff refused to make an order that the plaintiff hould be allowed to see and inspect the whole of the eport and other documents passing between the doctor nd the company's solicitors The plaintiff appealed

In the Court of Appeal on March 30 Lord Justice ingleton (dissenting) said that the purpose of this ranch of the law of privilege was to enable a litigant r a party to impending litigation to prepare his case Statements had to be taken and reports obtained rima facie, they were the subject matter of privilege The privilege was that of the litigant but it inured for he benefit of the one who had made the report. A tatement so given should, generally speaking be egarded for this purpose in the same light as if it were iven in court To make an order of the kind suggested vould be a departure from the recognised practice and vould have the effect of deterring potential witnesses rom giving statements to solicitors whose clients vere concerned in litigation He would dismiss the ppeal

Lord Justice Hodson said that the claim to privilege vas based on legal professional privilege The rivilege was that of the litigant and not of his witnesses s such. For the purposes of this application, the doctor nust be looked at as a proposed witness on behalf of the ompany In that capacity not only had he no privilege f his own but he was under no duty to assert the right f the company He his Lordship would allow the ppeal subject to the concession by the plaintiff that he order for inspection was to take effect only when the ction against the company for personal injuries was isposed of

Lord Justice Romer agreed that the appeal should be llowed Leave to appeal to the House of Lords was ranted

Negligence Claim Dismissed

In an action in which an orthopædic surgeon claimed a fee of £48 6s for treating a woman patient's broken ankle judgment and costs were given to the surgeon A counter-claim by the patient for damages for alleged negligence was dismissed [1]

The patient by profession a teacher of dancing, alleged that a month after setting her ankle in plaster the surgeon had forced her to walk upon it in his surgery he had removed the plaster and manipulated her foot, causing her great pain The surgeon said in evidence that the fracture had been a severe one, and permanent disability would have resulted whatever the treatment. He had heard nothing of the allegations against him until five years after the injury

Giving judgment the judge said that he was unable to accept the patient's story He was satisfied that there had been nothing in the surgeon's conduct with which he should reproach himself

Injury to Hæmophiliac

How far should a person be liable for the consequences of his own negligence? Should he be liable only for what might be called the "normal" consequences or should his liability extend further? A hæmophiliac, who suffered injuries which to a normal person would have been comparatively trivial, has been awarded £3000 agreed damages and costs in the High Court [2]

The plaintiff a 35 year-old man said that he had suffered all his life from hæmophilia and had been in hospital over two hundred times. While driving his van in the Old Kent Road London, in July 1953 he was involved in a collision with an ambulance belonging to the London County Council. The accident caused bleeding into the hip and knee joints and made him a good deal worse than before Judgment was entered against the London County Council and the ambulance driver

The cases on remoteness of damage are not easy to reconcile but it seems clear that, where negligence is established the defendant is liable for all the direct physical consequences of his unlawful act Liability is therefore not limited in such cases to the normal consequences The award of £3000 damages in the present case appears to be in line with that principle

Parliament

Transfer of Functions of the Ministry of Food

IN the House of Commons on March 28 Mr HARRY CROOKSHANK, Lord Privy Seal, explained that it was now proposed by order to merge the Ministry of Agriculture and Fisheries and the Ministry of Food The interest of the Ministry in the food and drugs legislation would in a subsequent order be allocated to the Minister of Health, who would have the primary responsibility for hygiene problems. The new Minister of Agriculture Fisheries and Food would deal with the regulations about the composition of food to safeguard health and to prevent fraud and the regulations about food labelling

Mr ARTHUR BLENKINSOP was uneasy that matters dealing with the composition of food to safeguard health should not go to the Ministry of Health He asked for a better explanation of the Government's intentions. Mr HEATHCOAT AMORY Minister of Agriculture and Fisheries and Minister of Food assured the House that the second order would be brought forward as soon as possible The intention was that the primary responsibility for cleanliness and hygiene should go to the Ministry of Health with one exception The primary responsibility for slaughterhouses, meat and milk and dairies regulations would more conveniently remain with the new Department of Agriculture Fisheries and Food But of course in all these matters regulations would have to be made jointly and there would be the closest consultation Primary responsibility for the new Food Hygiene Advisory Council it was intended should go to the Ministry of Health

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1. *Manchester Guardian* March 29 1955
2. *Ibid* March 22 1954

QUESTION TIME

Nuclear Radiation

Replying to a question, Sir WINSTON CHURCHILL, the Prime Minister, said that the Government had already invited the Medical Research Council to review the existing scientific information on the medical aspects of nuclear radiation and to prepare a report The report would cover the medical aspects of nuclear radiation, including the genetic aspects It would be published as a white paper

Mr ERIC FLETCHER asked the parliamentary secretary to the Ministry of Works, as representing the Lord President of the Council, what progress had been made in the investigations concerning the genetic effects of increased radioactivity due to the explosion of nuclear weapons, and when he expected that it would be possible to begin research on measures designed to counteract these effects—Mr J R BEVINS replied Research on the genetic effects of radioactivity is necessarily of a long term nature, but a certain amount of progress has been made and results are published in the scientific press as they become available The Medical Research Council's programme has, for the past eight years, included work on means of protection against the effects of radiation

Mr FLETCHER Does the Minister realise that the public are becoming increasingly concerned to know what British scientists feel about the precise effect on the future of the human race of these nuclear explosions, are anxious to have full information in a convenient form, and are also anxious that the Minister's department should be able to assure them that some research is being conducted into what counter measures can be taken?—Mr BEVINS The urgency of the work is well appreciated, and it is, of course, going forward on an expanding scale However, I am bound to say that none of the radioprotectors or regenerators that have so far been discovered have any effect on genetic damage to animals or human beings

Protection of Hospital Workers

Replying to a question, Miss PATRICIA HORNSBY-SMITH said that it was the normal practice of hospitals in the National Health Service to observe the recommendations of the British X-ray and Radium Protection Committee about protection and working conditions in X ray and radium departments This code of practice was, however, in some respects out of date, and the Minister of Health hoped to bring into operation shortly a revised code approved by the Radioactive Substances Advisory Committee which included a section on the disposal of radioactive waste

Allegation against M R C Refuted

Mr PETER FREEMAN asked the parliamentary secretary to the Ministry of Works whether he was aware that a number of cases had recently been brought to the courts of cat stealing on a large scale and that several people had been convicted for this offence, that these cats had been stolen for sale to medical research laboratories, as admitted in court, that the cost of the defence and the fines had in some cases been paid by the Medical Research Council and that they had employed the same counsel, details about whom have been sent to him, in most of the cases, what authority existed for the payment of such expenses out of public funds, how much had been spent on each of these cases in the last six months, and what action he proposed to take to prevent a recurrence of such incidents—Mr BEVINS replied I am glad to have the opportunity of stating quite unequivocally, that there is no truth whatever in the allegations against the Medical Research Council

In answer to further questions he added that the Lord President had been into the matter with the most meticulous care and he was satisfied that none of the suggestions contained in the question was based on evidence The barrister whose name was supplied to the Lord President by Mr Freeman had had no contacts of any sort with the M.R C Defendants in court sometimes told the truth and sometimes they did not

Mr Freeman said that he would raise the matter again at the earliest possible moment

Doctors' Telephones

Replying to a question, Mr IAIN MACLEOD, the Minister of Health said that he was not prepared to seek powers to ensure that general practitioners in the National Health Service should be available to their patients on the telephone But, pre judging any entirely exceptional case, it seemed him as a general matter of common sense that a oviding general medical services was not in a proper position to fulfil his obligations to visit his patients their condition so required if he did not make re arrangements for them to communicate with him by telep

Leprosy Treatment in the Colonies

Mr L W B TEELING asked the Secretary of State for Colonies how many leprosy hospitals there were in the C and in what Colonies patients with leprosy were refused mission, even when suitably accompanied, to visit towns from the leprosy centres—Mr HENRY HOPKINSON, Minister State for the Colonies, replied There is an institution for treatment of leprosy in every Colony in which the disease endemic, either in leprosy hospitals, outpatient departments general hospitals, or in separate settlements or villages. Con of patients under treatment with the general public is related the risk of infection in each case Mr TEELING Is the Mini aware that recently there have been so many discoveries w regard to leprosy that it is considered by those who a studying this disease that it is no longer really necessary have these completely isolated settlements? Will he m sure that the Colonial Office is keeping that in mind?

Dr BARNETT STROSS May we take it that it is n accepted that leprosy is not a dangerously infectious contagious disease and that free movement does not nec sarily bring danger to the community at large?—M HOPKINSON Yes, sir The danger depends, of course the specific case, but in the general way people still retain very serious dread of the disease Only education as to effects of modern drugs, and so on, will eradicate that fe

Obituary

GEORGE FORD PETRIE

M D Aberd

Dr George Petrie, lately retired from the staff the Lister Institute of Preventive Medicine, died at age of 81 on March 17

He graduated in medicine from Aberdeen Unive in 1898 and five years later took the M D with honours As an undergraduate he had shown lean towards pathology and was awarded medals in th subject After qualification he became for a time assistant in general practice till, in 1902, he was appoint assistant bacteriologist to the Lister Institute, w in the serum department at Elstree under the Dr George Dean In 1905 he served as a member of Plague Commission under the late Sir Charles Ma in India and again from 1911 to 1914 under Dr Ch Todd in Egypt During the first world war he commissioned in the R A M C and worked as a ge bacteriologist in France After the war he returned the Lister Institute, and in 1919 he rejoined the department at Elstree, of which he was ap bacteriologist-in-charge in 1926 From then until retirement in 1939 he carried out investigations into wide variety of bacteriological and immuno problems, and was responsible for the production standardisation of many antisera It was on the foundations laid by him that the large-scale producti of potent antitetanic serum was based During the war he came out of retirement for some years to re charge of the serum department of the Lister Institute

Dr Petrie's publications included many papers deal with epidemiological, bacteriological, and immun logical subjects In 1934 he published a book with late Sir Alexander Fleming on recent advances in vacc and serum therapy During his retirement he arrang an anthology of *British Medical Science and Practice*

C T writes "Petrie was a conscientious work He was a delightful companion with many interest particularly in natural history He was also a great read especially of the more classic English literature In earlier years he was an incessant smoker and someti in the middle of a meal he would absentmindedly li his pipe and go on talking, having forgotten all about next course During my long absence from England lost intimate touch with the details of his work, but managed generally to meet almost every year I sh miss him sadly"

Mr A F MACCALLAN, consulting ophthalmic surge to the Westminster Hospital, London, died on Mar 31 at the age of 82

In England Now

Running Commentary by Peripatetic Correspondents

THE sport of underwater swimming, fishing and photo-aphy is becoming the rage, with clubs devoted to it ringing up all round (one in this country is said to have thousand members) A spate of books and films, both tional and documentary, has stimulated Tom, Dick, d Harry with their wives and children, to emulate ans and Lotte Hass, Captain Cousteau and the Criles it is not surprising that the First International xhibition of Underwater Exploration and Photography now being held.[1] Most of the exhibits are photographs many familiar and some unfamiliar incidents from the ooks and films, and some show a few of the difficulties perienced by Walt Disney's photographers, one of hom had to stand on his head to adjust the camera. trange fishes (who will be the first to photograph the elacanthus in its natural habitat ?) and beautiful coral ardens abound and H G Vevers shows his carpet of rittle Starfish at Plymouth. Other exhibits include atertight cases to enable ordinary cameras to be used nder the sea, a watertight compass (presumably to revent taking the wrong turning) and watertight inoculars (as already used by bird watchers in marshes)

And last, but decidedly not least, there is, posing lternately in sea green and in snow white diving ostume and wearing frogman's flippers, a real live mermaid who made me want to visit Copenhagen to ind out if Hans Andersen's had become detached from er rock.

* * *

When the canal was frozen the rats having nowhere lse to go came to us. So I went to see the sanitary nspector who said if I put five bob down he would send chap round to get rid of them When I got home at unch time I said to my wife

Has Ratty come ?

' Yes

What's he say ?

" Nothing

So I went to have a chat with the Rat Man Rather posh chap with a corduroy cap very straight on his head

"I didn't like to say anything to your wife he said; ' women are easily upset but I don't think you ought to leave the child in the pram.

The child ?

Well you never know

Then he took me round the garden The place was like a Swiss cheese with rat holes

Well where do we go from here ? I said

I will bait the holes.

And that will be the end of them ?

" They don't die straight away That was the old method They would die near the hole and then the next rat would come along and smell a rat, so to speak, and wouldn't touch the bait. With this new bait they got internal hæmorrhage and die three or four days later

That's clever

" It was worked out in America

Well work it out here chum and I'll be grateful.

When Ratty came back on the following Thursday he inspected the bait and most of it had been taken

Has it been taken ?

Yes indeed. This is a very effective method

Where do they die ?

Well it *could* be in the house

In the house !

Could be Or it could be outside If they die in the house under the floor boards they won't smell unless they happen to be near hot pipes.

Shall we block the holes up now ?

No no I shall lay more bait and if that is touched there will still be more around

And how long does this caper go on for ? "

If it *does* go on it means the drains are fractured

Why bring in the drains ? That's expensive If they have to dig up the drains it'll cost a mint

"We can find out if the drains are fractured without having to dig them up by the smoke test

' Thank God

But it fills the house with very acrid fumes Your wife should be warned

If I warn her any more she'll be off '

' The smoke is blown down the w c. pan and if there is a fracture it comes up in the garden at the site of fracture

Sounds simple Go ahead and let me know the worst

I went in to the wife.

Have they gone yet ? " she asked

" Not quite He's going to fill the house with smoke '

What for ?

' To see if the drains are fractured "

Well I think it's ridiculous when we had rats in Rhos we put down traps and caught them

" That's out of date You must move with the times, old flower "

On the following Monday I met Ratty in the garden

Well what's the form ?

I'm very disturbed. They should have gone but they haven't The smoke test was negative '

" Well I'm not a pro at this game but I think all the holes should be plugged up right away The house will be in ruins if something doesn't happen

You could stop them up but you might be imprisoning live rats under the house and they will gnaw their way up through the floor boards, which would be undesirable '

So I went in to see my wife.

' Have they gone yet ? "

No Any minute now they'll be coming up through the floor boards '

My wife is a woman of few words. " Rats. she said.

* * *

We were gratified that our eldest son should be following in both our footsteps, and thought we might help him in his biology for first M B Primed with your leading article on Clonal Ageing we lately delivered at the breakfast table what we thought was a masterly account of the habits of the dimly remembered paramecium There was a disappointing lack of awe at our erudition Instead, as might have been foreseen, we are now referred to as ' the ageing clones.

* * *

Your leader on Man in Space was perfectly timed; for it was in my hands just ten days before my son aged 10, returned home for the Easter holidays. With what nonchalance was I able to meet the abrupt inquiry Dad do you know about the Heat Barrier ? "

But my relief was short-lived—for now I don't know which Heat Barrier Jonathan was discussing There is a band of heat around the Earth of a limit not given which holds toxic amounts of ozone and a high temperature not specified Further on we come to Space Space is not defined in this sense by my edition of the *Concise Oxford Dictionary*—I must get an *Encyclopædia Britannica*—but it has a vacuum temperature of 4000 F

It may be the step from the great cold into Space that Jonathan has in mind I think that this must be the Heat Barrier because I now learn that when you reach the Heat Barrier you are disintegrated, which is poor reward for having survived the discomforts, hazards, and minor sound, heat, and cold barriers earlier in the voyage

* * *

A somewhat fussy elderly lady came to see me after an interval of some years. I examined her; we exchanged the usual social chit-chat about weather and shortcomings of this year's sweet peas; she sat waiting for her E.C 10 Unfortunately I am a man who-never forgets-a face-but has no-memory for names I did not wish to offend an old patient; but I racked my brains in vain At last inspiration came to me I have forgotten how to spell your name ' I said innocently ' JONES the lady replied tersely and never returned to my surgery

* * *

Lines composed in the neighbourhood of the R S M on a weekday afternoon

Parking is such sweet sorrow
That I shall drive around and round
till it be morrow

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[1] In the gallery of the Royal Society of Painters in Water-Colours 26 Conduit Street W 1 from April 4 to 30

Letters to the Editor

GENETIC EFFECTS OF THERMONUCLEAR EXPLOSIONS

SIR,—Some of the more pessimistic views recently expressed on the genetic dangers of peace-time thermonuclear explosions are unrealistic They take no account of the eugenic counter-measures which mankind will surely take

No reliable figures for the effect of a given dose of radiation on mutation-rates in man are available, but it is not unreasonable to suppose, as you do in your annotation last week, that two explosions yearly might double the natural level of radiation and hence the mutation rate An increasing programme of explosions would have a correspondingly greater effect But this does not mean that the human species will undergo irreversible genetic deterioration

First there is the question whether an increase in mutation rate is harmful Some human geneticists believe that it is impossible to say whether a gene is "good" or "bad" in its effects A mutation lethal in the homozygous state may be beneficial in the heterozygous state Further, they claim that it is impossible to predict the future, so that a mutation now harmful may be useful in future environments These are not my own beliefs and so I will not elaborate them further It is, I think, probable that most mutations are harmful, that most of them are either recessive or dominants of low penetrance, and that ultimately the balancing by natural selection even of the present mutation-rate requires fairly high miscarriage, stillbirth, and childhood-death rates

Even so the dangerous effects of an increase in the mutation rate can be prevented provided that mankind is prepared to undertake control of his own evolution Surely a few groups at least of such a resilient species as our own will make this attempt some time in the centuries before the increased mutation-rate can cause a disastrous fall in average fitness The initiative will probably come, not from governments, but within individual alert and responsible families

The great potential effectiveness of such artificial selection depends on the fact that most mutations affect only a small proportion of those who possess them, the remainder being apparently healthy carriers This is the case whether they are mainly dominants of low penetrance or recessives exerting an effect only in the homozygous state Within the next century or so it will be possible to identify most of these genes in the carrier state This is already possible with the genes responsible for thalassæmia major, sickle cell anæmia, and one form of sex linked choroidoretinal degeneration Once symptomless carriers can be recognised it is possible to encourage them to plan a family size below replacement rate For example, if the heterozygotes for any rare recessively determined condition aim at a family size of only two children and thus have a fertility, say, of only three quarters of those homozygous for the normal gene at that locus, this will prevent any increase in the frequency of the gene concerned even though the mutation rate is increased, say, a hundredfold from 1/40,000 to 1/400

This is selection against a single mutation Selection against a great many mutations naturally means that selection against any one of them must be less intense We are probably all carriers of some deleterious mutations Once the knowledge is available the aim of artificial selection would be to lower the fertility of those with

total number of deleterious mutations But

mass selection can have considerable effect

tions are hypothetical One estimate, by H J Muller,[1] is that the present mutation rate would be balanced if the 3% of the population with the highest number of mutations did not have children A sliding scale relating the planned family size of each individual couple to the number of mutations they possess would be still more effective in eliminating mutations In a real emergency unorthodox methods of achieving highly selective reproduction will be available, such as the widespread use of artificial insemination with donor semen almost free from mutations

The task of determining how many mutations each individual carries is obviously a major one, it may well become one of the chief tasks of the family doctor But it is possible meanwhile that much could be done by purely phenotypic selection—a process which is already occurring among the groups who effectively plan the size of their families

Any talk, therefore, of the end of the human race from peace-time experimental thermonuclear explosions is unjustified, provided that man's knowledge of human inheritance advances and he is willing to apply it Even with current mutation rates, some artificial selection will ultimately be needed to maintain our present health standards Once the practice of such artificial selection is accepted it could keep the balance against considerably higher mutation-rates Even the danger of wa with thermonuclear weapons, to which Dr Summerskil drew attention so dramatically in the House of Common the week before last,[2] would seem to lie more in the los of our scientific knowledge of how to deal with th increased mutation rate than in the increased mutation themselves But if war seemed imminent it woul obviously be a prudent precaution to store considerabl amounts of germ-plasm in radiation proof container in the hope that survivors might retain the skill to us this rather than their own damaged germ-plasm fo reproduction

Orpington Kent C O CARTER

COUNTING THE SWABS

SIR,—Every surgeon will agree with Mr Riddell statement (March 26) that it is the instrument nurse duty, and hers alone, to count the swabs before and aft an operation The surgeon must take care that no loo swab ever enters the abdomen, that all small ones a on holders and all large ones have a corner or a tap to which a forceps is attached, lying outside the abd minal cavity At the conclusion of the operation h must ask her if the count is correct, and help her i the search if it is not But if he attempts to do th counting himself, that essential element in all safet precautions—the complete responsibility of one individu for each item—is lost

There may be considerable anxiety when the coun is not correct The surgeon makes a thorough search fo the missing swab It is not in the operation site It ma turn up between the towels and the patient's body wrapped round the specimen that has been sent to th pathologist, or even stuck between the sole and heel o the assistant's boot

I was faced with such a problem four years ago

After three counts and three careful searches in the abdomen one large swab was still missing The patient had by now had enough, and I was forced to close the abdomen I consulted my solicitors and was advised to tell the patient frankly that a swab was missing at the end of the operation, that I had searched for it, and that I did not think it was in the abdomen He was first incredulous, then deeply distressed His postoperative course was stormy He ran a temperature He and I felt (or thought we felt) a lump in the left hypochondrium However he made a slow, but satisfactory, recovery I saw him once a month for six months, and en at three-monthly intervals for two years, but the missing wab has never been accounted for

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[1] Muller H J *J hum Genet* 1950 2, 111

[2] See *Lancet*, April 2 1955, p 725

Anxiety over the missing swab has been largely olished by the use for small swabs at any rate, of auze into which an opaque strand has been woven hese radio-opaque sponges have been in regular use in merica for at least ten years and they are now available n this country Their use in the case I have recounted ould have saved the equivalent of ten years wear and ear on the coronary circulation of two people

London, W 1 HENEAGE OGILVIE

TUBERCULOSIS IN IMMIGRANTS

SIR,—I am reluctant to prolong a discussion to which ou have already given much space but I must challenge he inference which Dr Doig (March 19) draws from his igures of tuberculosis mortality and morbidity in the sland of Lewis

The percentages of tuberculin positive children even in owns, are not high; and it is quite usual in remote districts o find small areas in which there are many positive tuberculin eactors, among whom new cases of tuberculosis will appear nd who because they are so far from hospital and radiological facilities, may die of the disease It is not so long since Dr Doig was pointing out (Jan 15) that it was the tuberculin positive young adults from his island who developed tuberculosis when they left home to work, and he cannot be permitted to argue both ways If he is right however in his assumption that a high death rate from tuberculosis is consistent with a high tuberculin negative rate then Lewis is unique because elsewhere the opposite is true A typical example is in the Philippines, where over 50% of 3 year-old children, 80% of 10 year-old children, and 90–100% of adults over 20 react to tuberculin[1] Tuberculosis is the leading cause of death among Filipinos Palmer and Shaw[2] in an extensive investigation of the results of B C G vaccination, found a negligible number of new cases and deaths in vaccinated persons and in unvaccinated tuberculin negative controls but they found that morbidity and mortality from tuberculosis were almost confined to those who were naturally tuberculin positive at the beginning of the survey

The same applies to Ireland The idea that tuberculosis arrived here recently is quite fantastic it was recorded as a cause of death in Irish cities in the 17th century and I have no doubt that it was known much earlier The enormous increase in the population of Ireland between 1695 and 1841 from 1 million to 8 million was mainly in the rural population in tenant farmers and in labourers[3] The subsequent overcrowding and malnutrition made an epidemic of tuberculosis inevitable and the great famine of 1847 gave a tragic impetus to the disease throughout the 19th century Death and emigration reduced the population as rapidly as it had increased, and many rural areas which had formerly been congested became sparsely populated Regrettable as this was from a national point of view it had the effect of limiting the spread of infection and in recent years as Dr Flynn and Dr Joyce (Feb 26) rightly stated modern methods of diagnosis and treatment have reduced the amount of disease still further It is important to remember therefore that if many young people in the Irish countryside are tuberculin negative it is not because infection has not yet reached their districts, but because it has already left them Certainly in Northern Ireland and apparently in Eire as well tuberculosis in rural areas is no longer a problem of any size or importance It is prevalent only in the cities and large towns which for so long have been thoroughly tuberculinised and which contain the highest percentages of young positive tuberculin reactors[3]

The Irish are not the only immigrants amongst whom tuberculosis has been common. Plunkett[4] has drawn attention to the problem of tuberculosis among displaced persons from Europe who were admitted to the United States after the 1939–45 war In Israel the incidence of tuberculosis is now several times greater than it was in 1947 and this is attributable to indiscriminate mass immigration.[5] No-one would attempt to argue that displaced persons from Europe and Jewish immigrants in Israel were lacking in experience of tuberculous infection or to deny that they had taken their infection with them But Dr Hess and Dr Macdonald (Feb 12) believe without having carried out a single preliminary test that it is the tuberculin negative Irish who develop disease in England and it seems strange that too little infection in the native country should have the same effect as too much

I do not deny that individual or even racial susceptibility can vary or that social conditions will modify the incidence of tuberculosis for better or worse, but I do insist that the intensity of infection in any country is the decisive factor in causing tuberculosis and that the elimination of infection is at present the only means we know of preventing it Ultimately the immunising *fraction of the tubercle bacillus* will almost certainly be isolated but so far there is no convincing evidence that artificial "tuberculinisation" with B C G vaccine can succeed where the natural process has so obviously failed

The task of eliminating infection is difficult but no longer impossible and the goal before us in the United Kingdom is not merely the control but the eradication of tuberculosis The task is not made easier by those who point out spurious short-cuts upon which to waste energy and resources.

Dungannon Chest Hospital
Dungannon,
co Tyrone
E F JAMES

B C G VACCINATION

SIR,—The points raised by Dr Webster (March 5) and Dr Loxton (March 19) are, of course, of the greatest importance in arriving at any conclusion on the value of B C G vaccination Unfortunately our knowledge on immunity in tuberculosis is still very incomplete, and at present I do not think it is possible to state the relationship of tuberculin hypersensitivity to immunity, but many authorities believe that the former is an expression of the latter although the lack of hypersensitivity does not indicate an absence of immunity

B C G vaccination is based on the assumption that recovery from a primary tuberculous infection be it caused by virulent or by attenuated bacilli, confers a certain degree of acquired resistance to subsequent infections The degree of the acquired resistance conferred will vary from individual to individual, and the possibility of developing active disease after vaccination will depend on the age of the individual, the magnitude of the infecting dose and the cellular response to the invading bacilli I agree that the last phrase begs the question, and it is by making such statements that we 'go round the mulberry bush' of immunity

It is probable that a high state of resistance to tuberculous infection is present in persons who have become desensitised by repeated infections Evi for this is found in the state of tuberculin anergy tha is attained by some persons who have worked in a high infectious environment for many years and also by th state of 'positive anergy' in children who have bee given B C G orally over a number of years Sayé[6] in his vaccination work in Barcelona is able to produc by repeated oral vaccination a state that reacts ver feebly, or not at all to the jelly patch test but still be sensitive to $^{1}/_{10}$ mg of B C G given intradermally Sayé terms this *l'allergie atténuée* or *latente* and conside it evidence of the optimum degree of resistance state corresponds to Godlowski s second type as describ by Dr Loxton Whether this state is more immune t infection than the one of tuberculin sensitivity that w are producing by the usual method of vaccination i this and many other countries has not yet been de mined If it is so, then repeated B C G vaccination by the oral method does satisfy Dr Loxton's demand "for a vaccine which will confer immunity, and will, at the same time, desensitise the patient"

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[1] Vergara, J J Proceedings of the Pan Pacific Tuberculosis Conference, Manila, Philippines, 1953 p. 506
[2] Palmer C E, Shaw L W Amer Rev Tuberc 1953, 68 462
[3] Tuberculosis in Ireland: Report of National Tuberculosis Survey (1950–53) submitted to the Medical Research Council of Ireland Dublin, 1954
[4] Plunkett R E. Trans. nat Tuberc Ass. N Y 1952 p 493
[5] See J Amer med. Ass 1954 155 1519
[6] Sayé L. Pr méd. 1953 61 524

May I take this opportunity to correct what might give a wrong impression in my article (Feb 12)? I stated that the relapse rate to tuberculin anergy in Ireland is 20 72% On referring to the original work of the late Dr Dorothy Price,[7] I find that this figure included an exceptional group and that a more correct figure would be 11 8% over a period of two or three years' observation In addition to the reasons I stated for the reversion rate, I am grateful to Dr St John Cowell, the medical director of the National B C G Committee, St Ultan's, for reminding me that in Eire the Swedish vaccine is used on a rural population, and the Danish on an urban one, also that the follow-up at St Ultan's was for two or more years The chances of superinfection by virulent organisms in Dublin City are greater than in the rural areas, so the reversion to tuberculin anergy will be less frequent The fact remains that reversion is an important event, and the possibility of it must be continually borne in mind in B C G vaccination campaigns, particularly in infants and young children

Department of Tuberculosis,
Welsh National School of
Medicine Cardiff

FREDERICK HEAF

PURE RED-CELL APLASIA

SIR,—The case described by Dr Fountain and Dr Dales (March 12) provides another interesting example of the complexity of these unusual anæmias Their conclusion that oral cobalt therapy led to the patient's recovery could be of the greatest importance, and it will be most interesting to see, should the patient relapse, whether cobalt will again prove effective

I have given a solution of cobalt chloride (in daily doses of 100–300 mg) to two patients with "pure red-cell anæmia" This resulted in no improvement, but prolonged treatment was impossible because the patients seemed intolerant of the preparation There was certainly no immediate improvement, as in the case described by Fountain and Dales They cite the case reported by Seaman and Koler[8] in which cobalt therapy was of value in erythroid hypoplasia, though the patient did not improve until after 64 days of continuous cobalt treatment—a surprisingly long time when compared with other hæmatinics and the experience of Fountain and Dales

I wonder whether more credit should not be given by Fountain and Dales to the effect of splenectomy in their case It was followed by progressive increase in numbers of marrow erythroblasts for 3 months after the operation Apparent benefit from splenectomy was delayed for nearly a month in a somewhat similar case I have studied, and 4 months' delay for improvement in blood values after splenectomy is probably not impossible

Any means of treatment which will avoid repeated transfusions to such patients deserves energetic study Only recently a patient of ours (Chalmers and Boheimer,[9] case 1) died from hepatic cirrhosis and general siderosis although recovery from pure red cell anæmia had been complete for over 2 years and he showed no hæmatological relapse in his final illness He had previously received some 55 pints of blood at a time when erythropoiesis was absent In his terminal illness he did not want venesections performed, and it was tragic to see a death probably due to the late effects of a measure which had earlier been the sole means of keeping the patient alive

St George's Hospital
London S W 1

J N M CHALMERS

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[7] Price D S *Irish J med Sci* February 1954 p 56

[8] Seaman J Koler R D *Acta hæmat* 1953 9 153

[9] [illegible] N M Boheimer K *Brit med J* 1951, ii 1514

A LIVER POISON WITH UNUSUAL PROPERTIES

SIR,—Dr With has called attention (March 19) to the work of Quin[1] showing that administration of the South African plant *Lippia rehmanni* (verbenaceæ), or alcoholic extracts of the plant, to sheep causes inhibition of biliary secretion and consequent jaundice without evident hepatocellular damage He does not add that the active principle was later isolated by Rimington, Quin, and Roets,[2] and named "icterogenin" It was shown to be a triterpenoid acid and to arise in the leaves of the plant during active growth and to be translocated and stored in the fleshy root bark

Atony of the fore stomach and large intestine and bilirubinæmia regularly followed administration of 1 5 g of crystalline icterogenin by stomach-tube to sheep Fairly extensive pharmacological study showed that icterogenin inhibits the smooth muscle of the gut and the isolated, perfused heart It is mildly hæmolytic in vitro The jaundice which follows its administration by mouth is not hæmolytic, it seems, rather, that the pigment excretory function of the liver is temporarily impaired

Recently Barton and de Mayo[3] have further studied the chemistry of icterogenin and have completely elucidated its structure I am at present awaiting a new supply of material from South Africa with which the icterogenic property of the drug is to be investigated more fully in association with Dr G H Lathe and Dr B H Billing

Department of Chemical Pathology,
University College Hospital Medical
School London W C 1

C RIMINGTON

THE HAIR OF THE PILONIDAL SINUS

SIR,—Mr F E Weale (Jan 29) describes some ingenious histological investigations on the hairs of natal-cleft pilonidal sinuses, showing that they all lie with their roots deeply, and he concludes that "the sinuses are therefore developmental defects" His facts seem conclusive, but his conclusion depends on two assumptions (1) that this is what one would expect if the sinuses were developmental, and (2) that such an arrangement of the hairs rules out the possibility of an acquired origin

On the first point, there is no obvious reason why a developmental sequestration of skin should produce hairs running only in one direction, and Mr Weale's further assumption that the hair bearing is limited to a "fairly circumscribed area" at the cranial extremity of the sinus stretches the developmental hypothesis still further beyond what is reasonable

It is on the second main assumption that we wish particularly to comment There is a very clear explanation of why hairs should enter a natal cleft sinus with their root ends in advance One of our students—Mr E S Williams, B SC—has reminded us of the countryman's old trick of making a head of barley progress up someone's sleeve, merely by introducing it base first, and he has pointed out that the mechanics of propulsion of a hair are similar The scales of a hair are so arranged that their free ends point peripherally As a result, if a hair is stroked along its surface from the root to the periphery there is little movement of the hair, owing to the slight frictional resistance If, however, a hair is stroked from the periphery to the root, there is considerable frictional resistance from the free ends of the hair scales, and the hair is propelled in the direction of its root (One can readily confirm this by placing a hair in the palm of the hand and rubbing to and fro along its axis with a finger of the other hand)

Applying these mechanical principles to the natal cleft, shed hairs will naturally tend to lie longitudinally owing to the configuration of the cleft The normal frictional movements between the sides of the cleft will propel the hairs either cranially or caudally according to the direction in which root of the hair happens to be pointing If a sinus or is present many of the cranially propelled hairs will enter orifice invariably root first The same forces will resist expulsion of the hairs and tend to force their roots still her into the depths of the sinus. They may also drive infected hair into the intact skin and thus initiate a nidal sinus.

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[1] Quin J I *Onderstepoort J vet Sci* 1933 1 501

[2] Rimington C, Quin, J I Roets G S C *Ibid* 1937 9 225

[3] Barton D H R, de Mayo, P *J chem Soc* 1953, p 887

Jp till now the one flaw in the hypothesis of the quired origin of natal-cleft pilonidal sinus has been doubt on how the hairs got in We have in the st suggested a suction mechanism and it may be that is does play a part in the digital-cleft sinuses of barbers. it in the natal-cleft pilonidal sinus we now believe that vement of the hair under frictional influences, as scribed above, is the essential factor Mr Weale's servations on the lie of hairs in a pilonidal sinus by awing attention to the hair scales have thus indirectly 1 to the filling of the one important gap in the case r the acquired origin of natal-cleft pilonidal sinuses. the acquired origin of most other varieties of pilonidal nus there has never been any doubt.

The Middlesex Hospital,
London, W 1

DAVID H PATEY
R W SCARFF

HYPOTHERMIA IN THE NEWBORN

SIR —I was very interested to read Dr Trevor Mann s tter in your issue of March 19 I agree with Dr mallpeice and Dr Everley Jones (March 26) that this ndition is no new one I have seen 24 cases in the last n years and they have all been in the winter months ovember 1 December, 8 January 5 February, 8 arch 2

Like Dr Everley Jones I call the condition sclerema eference to textbooks on the disease is disappointing t is usually dismissed in a very few lines as a rare and lmost invariably fatal disease with no seasonal incidence t certainly is not very rare many of the cases recover nd the seasonal incidence is marked

Sclerema is always present I too have purchased a low reading thermometer and the following are the emperatures recorded by me 90 5 90·4 91 90 87, 93 8 84, and 86°F

The treatment that I usually give is thyroid extract r $^{1}/_{16}$ three times a day vitamin E 5 mg daily, peni illin and warmth The majority of the babies survived I know for certain of only 5 deaths but my records are incomplete I was not aware of the danger of rapid heating and I hope that in future more temperate treatment will produce even better results

Leicester

J VERNON BRAITHWAITE

SIR —Dr Trevor Mann has performed a useful task in drawing attention to the syndrome of hypothermia neonatorum We also see a few such cases each year Although they all occur during the winter months, it is not always easy to correlate the development of the syndrome with a cold environment The rooms in which the babies have been kept have sometimes seemed to be adequately warm nor have the cases always arisen during very cold weather My last one developed during the thaw that followed a cold spell The relationship between hypothermia and sclerema is also somewhat inconstant in my experience I have had cases of severe hypothermia without sclerema and of sclerema without hypothermia

I would entirely endorse Dr Mann's remarks regarding the danger of warming these babies too rapidly but I have found that small doses of thyroid extract are beneficial

D A J WILLIAMSON

Royal Hampshire County Hospital,
Winchester

SIR,—I read with interest Dr Mann s communication I wonder if he would consider trying to warm these babies by the technique described by Khalil and Mac Keith [1] They insert into the stomach a plastic tube with a rubber balloon attached to the end Warm water is injected into it and withdrawn at intervals after it has had time to supply heat to the body—i.e to the large vessels adjacent to the stomach The method was actually used to lower the body temperature of a hyper pyrexial child but the authors state that it could be equally well used to supply heat and they suggest that it has several advantages over the method of warming patients by external heat

Keats House,
Guy's Hospital
London S E.1

PAUL E POLANI

RUPTURE OF LAPAROTOMY WOUNDS

SIR,—Three weeks ago, at the conclusion of a partial gastrectomy, the aponeurotic layer of my abdominal wound was closed with interrupted sutures of nylon (no 7) sterilised by the normally approved methods. Forty-eight hours later a cough of very moderate violence caused every suture to snap at a point well clear of the knot There was no staining of the dressing either then or at its later removal, but a patch of surgical emphysema appeared on the left anterior thoracic wall giving a clue to what had happened Successful resuture with linen thread followed

This experience makes me doubt whether nylon is so perfect a suture material as is claimed by Mr Mill (March 26) If Mr Mills consults the fishing periodical of the past seven years he will find a voluminous and acid correspondence on the erratic tensile strength o nylon and certainly I cannot enthuse over a material which holds neither my fish nor my anterior abdominal wall.

London, S W 7

FRANK GREENWOOD

CONGENITALLY SHORT FRENULA OF UPPER LIP AND TONGUE

SIR,—We should like to congratulate Mr Michae Oldfield (March 12) on his exposure of two myths firstly that ' there is no such thing as tongue tie and secondly that operations on frena of tongue or lip are unnecessary and useless These two common errors arise we feel sure from two sources students are rarely, if ever taught anything about the matter and on referring to a textbook they find such negative sentences as above which have probably been copied from edition to edition without thought or verification

Operations almost identical with those described by Mr Oldfield have been done routinely at this hospital for many years when indicated To those who doubt the necessity for these little operations we would say ' try yourself to say D or T with the tongue held no higher than the lower incisor teeth ' It is quite impossible nor can L or S be pronounced clearly Take any short sentence and note how frequently these sounds are required to render speech intelligible

The frenum labii certainly sometimes causes an unsightly space between the central incisor teeth and is also the cause sometimes of an ugly sibilant lisp in speech If the frenum is abnormal it should be treated as such The teeth will come together and speech become normal—provided it is done in time and not left until adolescence Dentists sometimes say that this operation is unnecessary because the space can be eliminated by an orthodontic appliance but if the abnormal frenum persists the teeth will revert. Operation takes much less time and is more certain There is only one point on which we are not in accord with Mr Oldfield—namely, in the use of intra tracheal anæsthesia for young children

Several workers have pointed out the risks of tracheal trauma and the formation of a membranous plug and we agree Fine intranasal catheters passed to the pharynx are, we find, excellent and sufficient for such short anæsthesias, with the head dropped low no pharyngeal packing is necessary, and if one is sufficiently quick with mosquito forceps there is no loss of blood whatever Treated thus the patient need not be in hospital more than a few hours

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[1] Khalil H H MacKeith R C. *Brit. med. J* 1954 ii, 134

' Simple division, we agree, is useless—recurrence is the rule One typical case we would cite

' A boy, aged 8, had very defective speech He had been seen by several doctors, and his mother had been told that all authorities were agreed that there was no such thing as "tongue tie", he had also had courses of speech therapy without improvement On examination an extremely short frenum linguæ was obvious His tongue could not possibly make tight contact with his palate for L, D, T, and S An operation essentially as described by Mr Oldfield was done, and with very little instruction he quickly spoke quite normally How much better, though, if the defect had been discovered in infancy and all his mother's worries and his own troubles at school had been avoided

Bassam Hospital
near Wellington, New Zealand

CECILY M PICKERILL
H P PICKERILL

ENURESIS

SIR,—Your leading article (Feb 19) and the subsequent correspondence emphasise that enuresis is a symptom in which conventional concepts of medicine are inadequate Physiological, pathological, or psychopathological investigation separately will not give the whole picture, though many useful observations have been made by such means

Enuresis is a good example of an illness that should be studied "as a patch of personal biography," and as such it may go beyond the individual We should not pay undue attention to the mechanics of micturition unless there is a structural abnormality or some other relevant lesion Enuresis is more often found to be evidence of tension in relationship between the patient and his family, hence the number of instances where a child is enuretic at home but not when visiting or on holiday

Dicks[1] has said "Modern child psychiatry has long recognised that stress in a family cannot be compartmentalised We know that the whole unit is involved, even though only one member may present himself as a patient" The fact is that our investigation and understanding of the problem should go beyond the boundaries of the individual concerned "Cure" takes place with many therapeutic procedures Sometimes one patient may be "cured" only for another member of the family to take on the weight of the family disturbance with quite a different symptom

Department of Psychiatry,
University of Leeds

J H KAHN

INACCURACY IN THE LABORATORY

SIR,—Dr Bassir's letter (March 26) welcoming freeze dried samples of blood-serum is liable to occasion some misconceptions

Firstly, the freeze dried serum is not intended as a replacement of the standard solution in any method the intention is to provide a serum containing certain constituents in known concentration wherewith a laboratory can assess the extent of the inaccuracy with which a given determination is carried out

Secondly, the international survey with similar material carried out last year was not available to all laboratories, and, because the results were not available until some time later, was unlikely to be very useful to the individual laboratory as a control of the standard of its work. The object of the international survey was to confirm that the results of a given determination on a given serum vary considerably from one laboratory to another, this was already well known in this country and in the U.S.A, but it may be that the survey served a useful purpose in convincing some European pathologists

One can only agree with Dr Bassir that a thorough overhaul of our existing methods, apparatus, conditions [illegible] and so forth is desirable, with the object of detecting and eliminating the causes of inaccuracy Dr Bassir asks whether the clinical value of the laboratory warrants such an effort If laboratory investigations are to be carried out at all, the results should be sufficiently accurate to be clinically useful, the various surveys have revealed that in many laboratories such a standard is far from being achieved

Sheffield

ARTHUR JORDAN

MENTAL HEALTH AND PUBLIC HEALTH

SIR,—Dr Cameron asserts (March 12) "There is mention of psychology in the syllabus of general trainı of the General Nursing Council for Scotland"

Yet on p 6 of the syllabus there is a main heading, Hum Relationships, with six subheadings, and on p 13, under t heading, Mental Disorders, there are subheadings on t relationship between physical and mental illness, psych somatic disorders, psychoneurosis, and psychosis

Again, by quoting a single sentence from an addre by myself, he gives a false impression of the amount instruction in the psychology of development and alli subjects provided for nurses taking the subseque training for the health visitors' certificate

In Aberdeen a mental health course was recently organis to bring the knowledge of the older health visitors up to t level of their more recently trained successors this cou lasted for over 40 hours, despite the fact that even these ol health visitors were not at the start of the course complet without psychological training

Dr Cameron has really provided no evidence to refu the conclusions of the London Study Group

Health and Welfare Department,
Aberdeen

I A G MACQUEEN

ERETHISM

SIR,—In his most interesting article (March Dr Aldren Turner mentions that the term erethism likely to have been coined not from ἐρυθρός but fro ἐρεθίζειν

There can be no doubt about the etymology of erethis which is almost the transliteration of the Greek *ἐρεθισ* (excitation, irritation) Nevertheless the word erythism been used with the same meaning, and thence the suggest of *ἐρυθρός* as its possible derivation This, however, wo be not only highly irrelevant and inappropriate, but a verbally incorrect, for the English word should be erythri —a meaningless monstrosity

Yet even erethism is not a very fortunate term for t condition it is meant to describe, as it denotes a (consta state of excitation and not a morbid increase of the corr ponding quality Thus, while in English texts the wo irritability is used in connection with erethism, the Gre textbooks use the word *ευερέθιστος* (hyperexcitable)

Unfortunately the term is now well establishe and there is little hope of correcting it

Bethlem Royal Hospital
Beckenham Kent

G M JACOBIDES

HANDWRITING AND THE PSYCHE

SIR,—Your annotation (March 26) reads as if no wor had previously been done on this subject There is a va literature on handwriting by Continental and America authors Everything mentioned in your article is know to students of handwriting who are acquainted with th work of M Pulver and J Jacoby—to mention only two

Handwriting is an expression of the personality including its development or deterioration Neurotic o psychotic trends are detectable by those who know the job I remember Jacoby showing us the signature o Hitler, which had been smuggled out of Germany durin the last stage of the war, and the disintegration, compared with earlier specimens, enabled Jacoby to detect the mental decline which was confirmed by later event

London W C 1

E F MEYER

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[1] Dicks H V *Lancet* Feb 5, 1955, p 295

IRST-AID TREATMENT OF HEAD INJURIES

IR,—In your annotation of March 26 you make a eralised statement about first-aid manuals, which, n say ignore ' modern knowledge regarding the causes death after head injury the grave dangers of inhala n asphyxia in the unconscious patient have not yet ered into these manuals."

It is a pity that you did not refer to the instructions. ven in the *British Red Cross First Aid Manual* No 1 0th ed. 1952) There, on p 226, the general rules for st aid treatment of unconsciousness read as follows :

> Lay the patient *on his side* with uppermost leg flexed at p and knee, or face downwards with head to one side to event any vomit or blood from entering the windpipe and keep the tongue clear of the airway

London HAROLD E WHITTINGHAM

SIR,—The importance of maintaining a clear airway the unconscious patient is one of the primary duties the first-aid worker This is laid down in the manual n *First Aid to the Injured* (40th ed , p 162), issued by e St. John Ambulance Association :

> General rules for treatment of insensibility :
> (1) In cases of asphyxia perform artificial respiration.
> (2) If breathing is present, lay the patient on his back with head turned to one side
> (3) Do not leave the patient until he has been placed in the charge of another responsible person

As a divisional surgeon I have emphasised these points n my lectures for years. In first-aid competitions I have een candidates lose marks heavily for omitting obser ation of them. This makes it difficult for me to agree with our statement that first aid manuals give instruction hich ' ignores modern knowledge regarding the causes f death after head injury '

London, W 1 GILES ROMANES

*** The passage quoted by Sir Harold Whittingham is nfortunately followed by the words 'Alternatively lace patient as in fig 100 ' Here we see an illustration f the patient laid flat on his back with his head to one ide (see also p 228 of Red Cross manual) as is also dvocated by Mr Romanes in his letter This position s undesirable after head injuries (1) because it does not rovide adequate postural drainage, and (2) because otation of the head and neck can be very dangerous if as is by no means rare) the patient has a broken neck s well as a head injury.—ED L

METALLIC POISONS AND THE NERVOUS SYSTEM

SIR,—May I add these brief details of two British cases of industrial lead poisoning in adults which have been treated with calcium ethylenediamine tetra-acetate (E D T A.) to the three American cases cited by Dr Aldren Turner (March 26)

CASE 1 —The patient was a man, aged 42 who was employed in a lead smelting works on a refining process. He was seen by his private doctor who diagnosed lead poisoning but on arrival in hospital was thought to be a surgical emergency When seen by us twenty four hours later he gave a history of a similar illness, which had been called lead poisoning some years before when in the same work.

He was lying still, pale and trembling, and in obvious pain round the umbilicus His bowels had not moved for four days, and he occasionally vomited yellow fluid. He was edentulous with no blue line and his abdomen was soft. His hæmoglobin was 68% While calcium E.D T.A. was being obtained from a distant town he was given an immediate intravenous injection of calcium gluconate followed by two subsequent injections. By the time the calcium E D T.A. arrived the pain had gone but 1 g dissolved in 600 ml. 5% sterile dextrose in distilled water was given twice daily for five days

CASE 2 —The patient had complained of gradually increasing abdominal pain for three weeks, with vomiting and constipation. The pain was gripping and ill localised, and tended to move from the centre towards the right of the abdomen He had passed no motions or wind for two days. He was employed in a shipyard ; his work was to pile old paint tins, light a fire beneath them, and then, after the paint had been burned off scour them out with a wire brush A dust-mask was provided by the management but was not used

The patient had a good colour his tongue was furred ; he had upper dentures but his own lower teeth with a well marked blue line His temperature was 99 9°F, and he was tender in the right iliac fossa. He had a left nephrectomy scar Surgical opinion was that he had no acute surgical condition. His hæmoglobin was 82%. He was watched for twenty four hours, during which his condition appeared to be improving, and was given the same dose of calcium E.D T.A. as in the first case He made an uninterrupted recovery

In these two cases the total dose of calcium E.D T.A. was only 10 g , compared to 30 g reported by Foreman et al [1] but it was given at 2 g per day, as in their cases. This treatment led to clinical recovery without complications

Nuffield Department of
Industrial Health,
University of Durham R. C BROWNE

MELANOPHORE-EXPANDING ACTIVITY OF HUMAN PITUITARY GLAND

SIR —Dr Fraser (March 5) suggests that the melanophore-expanding substance which we have demonstrated in human pituitary tissue may be adrenaline There are three reasons why this is unlikely

We have never been able to demonstrate that adrenaline behaves like corticotrophin or melanocyte-stimulating hormone with respect to oxycellulose Nor have we been able to show that the *Xenopus lævis* used in this laboratory are particularly sensitive to adrenaline Doses of the order of 100 µg are necessary to produce detectable darkening and these are usually associated with marked mucus secretion by the animals. The pituitary extract which we prepared caused no secretion of mucus and produced a darkening in considerable excess of that caused by adrenaline.

Baker Medical Research Institute and
Alfred Hospital Clinical Research Unit
Melbourne, Victoria Australia. BRYAN HUDSON
G A BENTLEY

CONCOMITANT GASTRIC AND DUODENAL ULCERS

SIR —In my recent article (Feb 5) I said that the well recognised association between duodenal ulcer and hiatus hernia had not been explained

I then pointed out that the occurrence of heartburn in patients with duodenal ulcer was an indication that gastric retention and œsophageal reflux were occurring I went on to suggest that reflux œsophagitis by causing spasm of the longitudinal muscle of the œsophagus, in due course dragged part of the stomach into the chest.

I have since re-read the chapter on reflux œsophagitis in R. H Franklin s monograph on the œsophagus,[2] and I find that, though he does not go so far as I did in expressing the view that all hiatus hernias with short œsophaguses are preceded by œsophagitis and caused by spastic œsophageal shortening he does describe the association between duodenal ulcer and reflux œsophagitis and clearly explains how this may increase if not initiate the gastric herniation.

Plainly this was the source of what I mistakenly thought was my own idea and I regret not having recognised and acknowledged it at the time.

London, W 1 H. DAINTREE JOHNSON

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[1] Foreman H , Hardy, H L. Shipman, T L. Belknap E. L *Arch indust Hyg* 1953 7 148.

[2] Surgery of the Œsophagus. London 195*

Notes and News

University of Leeds

The following degrees and diplomas have recently been conferred

M D—Richard Burwell (with distinction)

M B Ch B—Bryan Dawson, M S Losowsky (with second class honours) J D Atwell, P M Binns J M Challinor Aileen A R Collinson Patricia J Corley, R C Cotton A D Crew, D W Daly, David De Souza, Jean McG Exley R F Folkes Margaret E Hall Brian McKibbin Dorothy Mainwaring D B Marshall Geoffrey Mitchell M J Oldroyd J F Poppleton, Ethel A Richardson, J B Richmond Juno M. Roberts Heather Sanderson, D R M. Stuart P H Tattersall C M. Tonks P J Truesdale, Evelyn Walker, Jean L Ward, Geoffrey Warnes, D A Youdale

D P H—Roy Barnes Ruth M. Bowker E P Griffiths, Diana J Halste I H Lewis J P Neylon A R Robertson

D P M—Harold Ellett Brown D McC MacGregor, A H Moyes, Narayana Chiruvolu Surya, R W Whiteley

University of Liverpool

The degree of CH M has recently been conferred on L F Tinckler

Royal College of Surgeons of England

The following Hunterian lectures are to be given at the college, Lincoln's Inn Fields London, W C 2 on Tuesday, April 19, Mr John Foster will speak on current methods of treatment of idiopathic stricture of the valve of Krause, on *Thursday, April 21, Mr Norman Barrett* will speak on primary tumours of rib, and on Thursday, April 28, Dr W T Cooke will speak on nutritional and metabolic factors in the ætiology and treatment of regional ileitis All the lectures will be held at 5 P M

Royal College of Physicians of Edinburgh

Karl Duncanson Fellowship for Medical Research—The council of the college is shortly to make an award for this fellowship (£600 for two years to begin on Oct 1) Applications must be sent before May 7 to the secretary of the college, 9, Queen Street, Edinburgh, 2

Christian Medical Fellowship

This fellowship is to hold house-parties for doctors and their families from May 6 to 9 at Windermere, and from May 20 to 23 at Bournemouth Further particulars may be had from the secretary, 39, Bedford Square, London, W C 1

Royal Statistical Society

Study Circle on Medical Statistics—On Tuesday, April 26, at 6 P M, at the Westminster Medical School, Horseferry Road, S W 1, Dr J N Morris will speak on Hypotheses on Coronary Artery Disease

Wessex Rahere Club

A dinner of this club will be held at the Royal Clarence Hotel, Exeter, on Saturday, April 30 Membership of the club is open to all Barts men practising in the West Country Further details may be had from Mr A Daunt Bateman, the hon secretary, 11, The Circus, Bath

Health Education Summer School

The summer school for 1955 organised by the Central Council for Health Education will be held at Bangor, North Wales, from Aug 16 to 26 The theme will be Opportunities and Methods in Health Education Applications should be sent to the medical director of the council, Tavistock House, London, W C 1

Orthopædics in Scotland

Since the Scottish Orthopædic Council was set up in 1942 it has distributed on behalf of the Lord Nuffield Fund for Cripples over £24,000 to orthopædic clinics, educational establishments for cripple children, and other aids to cripples in Scotland In addition the Nuffield trustees have made grants of £26,500 for hospital developments at Philipshill, Busby, and Princess Margaret Rose Hospital in Edinburgh The council has now agreed to dissolve since "orthopædic services were now firmly established in all five regions of Scotland, and therefore the work for which the Council had been formed had been accomplished" As part of the winding up process the Nuffield trustees have agreed with the council to allocate £15,000 for the erection of occupational therapy and workshop departments at the proposed spinal injuries unit at Edenhall, Musselburgh, and to make a grant of £2000 towards the extension of the residential training establishment for severely handicapped girls at Anton House, Broughty

Doctors and the Press

At an exploratory meeting between representatives of the Press organisations and the medical profession, held at British Medical Association House on March 29, it was decided to set up a committee to examine the relations between the Press and the medical profession, and to formulate proposals for further consideration The following doctors were appointed to the committee Dr H Guy Dain, Sir Harold Boldero, Dr R Forbes, Dr F Gray, Dr J G M Hamilton, Mr J R Nicholson Lailey, Dr. A. Talbot Rogers, and Dr W Woolley The first meeting will be held on Wednesday, April 27

Diary of the Week

APRIL 10 TO 16

Wednesday, 13th

ROYAL SOCIETY OF MEDICINE, 1, Wimpole Street, W 1
4 30 P.M *Physical Medicine* Dr E J Crisp, Dr J H Cyriax, Dr Basil Christie Treatment of Backache by Traction.
ROYAL INSTITUTE OF PUBLIC HEALTH AND HYGIENE, 28, Portland Place, W 1
3 30 P M Dr A I G McLaughlin Dust Diseases in British Industry
HARVEIAN SOCIETY OF LONDON, 11, Chandos Street W 1
8 15 P M Sir Adolphe Abrahams, Sir Arthur Porritt, Dr Roger Bannister Medical Aspects of Athletics
ASSOCIATION OF CLINICAL PATHOLOGY
2 P M (Palais de Danse Douglas, Isle of Man) Opening lectur *of four-day meeting*

Thursday, 14th

ROYAL SOCIETY OF MEDICINE
8 P.M *Neurology* Dr W R Bett, Prof Frank Goldby, Mr L C Oliver Dr Hugh Garland In commemoration of Jame Parkinson (1755–1824)
INSTITUTE OF PSYCHIATRY, Maudsley Hospital, Denmark Hill S E 5
5 30 P M Prof H McIlwain Maudsley, Mott, and Mann on th Chemical Physiology and Pathology of the Mind

Friday, 15th

ROYAL SOCIETY OF MEDICINE
5 P M *Epidemiology and Preventive Medicine* Dr Ira V Hiscoc (Yale) Changing Concepts in the Control of Tuberculos in the United States
INSTITUTE OF LARYNGOLOGY AND OTOLOGY, 330, Gray's Inn Roa W C 1
3 30 P M Mr William McKenzie Surgical Treatment Deafness
BIOCHEMICAL SOCIETY
11 A M (University of Liverpool) Opening of two day meeti with the Association of Clinical Biochemists

Appointments

CANNON, P G M B St And, D P H asst county M O and M O borough of Beccles, the Bungay Halesworth, and Leist urban districts and the Blyth and Wainford rural districts
HOPKINS G B, M B Birm, D.P H asst M O and district M O area No 7 (Downham urban district, Downham rural distri and Marshland rural district), Norfolk County Council
INGHAM, MARGARET, M B Birm, D C H asst M O.H Wolve hampton
MAKEY, A. R M.S Lond F R C.S part time asst surgeon Chari Cross Hospital, London
OWEN, KENNETH M B Lond, F.R C.S asst director surgic unit St Mary's Hospital Medical School, London
SCHURR, P H M B Camb, F R.C S neurosurgeon, Guy's Maudsl Neurosurgical Unit, Maudsley Hospital, London
SLEIGH JOHN M B Aberd, D P H deputy M O H, deput principal school M O, and deputy port M O, Newpor Monmouthshire
SYLVESTER D G G M.D Lond resident M O the Middlese Hospital, London

East Anglian Regional Hospital Board
CULLIGAN J D, L R C P I anæsthetic registrar, East Suffol and Ipswich Hospital
ESSEX LUDLOW M R C S anæsthetic registrar, West Norfol and King's Lynn General Hospital
JATOI A M M B Bombay surgical registrar, West Norfol and King's Lynn General Hospital

Colonial Medical Service
FAWKES M A, M B Camb, D P H M.O H, Federation Nigeria
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SANTOS W A, L R C P I superintending M O (specialist), Trinidad
SHORT R C M B Witwa'rand M O, South Pacific Health Service Fiji
WILLIAMS J C L.R C P I M O H Jamaica

THE URÆMIAS *

G. M. BULL
M.D. Cape Town, F.R.C.P.
ROFESSOR OF MEDICINE IN THE QUEEN'S UNIVERSITY, BELFAST

(concluded from p. 736)

PRINCIPLES OF TREATMENT

The uræmias arise because of an imbalance between he rates of intake or production of chemical substances n the body and their rates of excretion by the kidney t is clear from this concept of imbalance that we have vailable two main lines of therapy: we may improve enal function, if that is possible; or we may so adjust he intake or the production of chemical substances that normal balance is achieved despite reduced renal unction The main lines of treatment are

Adjust intake and rate of endogenous production of chemical substances to balance their rates of excretion when the kidneys are working at their maximum efficiency

(1) IMPROVE RENAL FUNCTION
  (a) Specific therapy depending on the cause
  (b) Correct circulatory renal insufficiency
(2) ADJUST INTAKE AND RATE OF PRODUCTION OF SUBSTANCES
  (a) *Reduce Katabolism*
    (1) Combat infection.
    (2) Hormone therapy
    (3) Protein-sparing diet.
  (b) *Adjust Intake of H_2O Na K Cl and N*
    (1) To correct imbalance
    (2) To maintain balance
(3) TREATMENT OF SYMPTOMS
  Anæmia, nausea and vomiting stomatitis, diarrhœa convulsions, insomnia, delirium hypertension.

Measures to Improve Renal Function

Many disease processes may reduce renal function and therapy will depend on the type All may be placed in one of three groups—obstructions true renal lesions, and circulatory renal insufficiency (extrarenal uræmia) The treatment of the obstructions is obvious In the second group, due to actual kidney damage, treatment is less satisfactory In some varieties such as acute pyelonephritis specific therapy is possible and in others, such as the hypercalcæmias and other toxic nephropathies improvement may take place when the cause is removed In the majority, however no specific treatment is yet available The third group—the circulatory renal insufficiences—is so important that it will be considered in more detail

Circulatory renal insufficiency is a better term than the older extrarenal uræmia because it indicates how is type of failure arises. Whenever the general circula on becomes inadequate for any reason the distribution blood flow through the body is altered circulation rough less vital areas is reduced while circulation rough the brain and heart muscle is relatively little fected The kidney which normally receives about a fth of the total cardiac output at rest now receives uch less; and as its function depends on a high rate blood flow renal failure results—circulatory renal ilure The primary cause is the general circulatory isturbance and this may arise either because of heart ilure (pump failure) or because of peripheral circulatory ilure (insufficient filling of the pump) All grades of enal insufficiency may be seen including complete bsence of renal function and death may result Circu atory renal insufficiency in its pure form recovers rapidly and completely on restoration of the general circulation and is one of the most satisfactory causes of the uræmias to treat

It is very important to remember that combinations of circulatory renal insufficiency with the other two groups of renal failure are common

For example a patient with chronic diffuse glomerulonephritis may develop congestive cardiac failure because of the accompanying hypertension and as a result, have a further reduction in renal function Treatment of the congestive cardiac failure will considerably improve renal function (table II) Another patient with a similar chronic renal lesion may lose water and salt by vomiting or by diarrhœa, or because of an osmotic diuresis, and so develop oligæmia with consequent circulatory failure further lowering his already reduced renal function Treatment will improve him considerably Fig 15 illustrates a case of this type

TABLE II—IMPROVEMENT IN RENAL FUNCTION AFTER TREATMENT OF CONGESTIVE CARDIAC FAILURE

Sign	Nov 15 1948	Nov 26 1948
Right auricular pressure (cm. above sternal angle)	+ [illegible]	−4
Cardiac output (litres per min.)	2 8	4 8
Effective renal plasma flow (ml. per min.)	41	95
Glomerular filtration-rate (ml per min.)	15	27
Blood urea (mg per 100 ml.)	190	90

The only treatment given between these dates was digitalis and rest in bed

Much the same may happen after release of urinary tract obstructions Water and salt may be washed out on the flood of an osmotic diuresis, so causing oligæmia Temporary improvement follows the release of the obstruction and then circulatory renal insufficiency sets in

Not only may renal lesions cause circulatory insufficiency, but the reverse may happen Any severe or long standing circulatory insufficiency may cause such a degree of oxygen lack in the kidney that the renal cells die, giving the histological picture of acute tubular necrosis

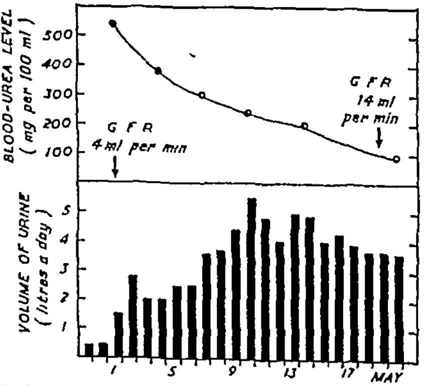

Fig 15—Effect of correction of circulatory renal insufficiency in a patient with chronic renal disease.

This patient with chronic pyelonephritis, was in a severe state of circulatory renal insufficiency as a result of losing salt and water in his urine and from vomiting Rehydration improved his renal function The glomerular filtration rate rose from 4 ml per min to 14 ml per min. and he lived for two more years, working most of the time

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The Goulstonian lectures for 1955 delivered before the Royal College of Physicians of London on Jan. 18 and 20 Based on work done with Dr A. M Joekes, Dr K G Lowe and Miss B M Evans at the Postgraduate Medical School of London and with Dr R N Bock, Dr R A Womersley and Miss E Martin at Queen's University and Royal Victoria Hospital Belfast.

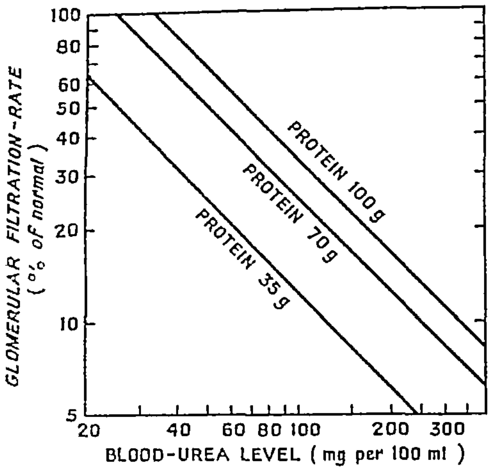

Fig 16—Approximate relation between blood urea level and glomerular filtration rate at different levels of protein intake in patients in a state of equilibrium between intake and output of nitrogen

Circulatory renal insufficiency, due to cardiac failure, is easily recognised, and its treatment well known Oligæmic circulatory insufficiency is linked with disturbances in water balance, and its management will be considered later

Thus, in every patient, we must determine the cause of the renal failure before we can attempt to improve renal function Obstructions should be relieved, and other recoverable causes of renal dysfunction sought and treated Above all, we must recognise circulatory renal insufficiency, even when combined with other causes, and treat it vigorously because it is the most amenable to treatment, and because it may lead to a more intractable type of renal failure

Adjustment of Intake and Rate of Production in the Body of Important Chemical Substances to Match their Rates of Excretion

REDUCTION OF KATABOLISM

The rate of production in the body of chemical substances, and the rate of migration of certain intracellular substances, such as potassium, into the extracellular fluid, are related to the rate of katabolism, which in turn is greatly affected by infection and is under the control of hormonal factors and the diet We should therefore attempt to reduce katabolism by controlling infections, by administering suitable hormones, and by diet

Control of Infection

Infection is an important cause of death in renal failure, particularly acute renal failure Because of this I now follow Merrill (1953) and his team in isolating these patients and using a form of barrier nursing All who come into contact with them should wear masks and gowns In addition, I prescribe, as a routine, 0 5–1 0 mega-unit of penicillin per day Because of the virtual absence of renal function, this can be given as a single daily injection of a crystalline salt

In chronic renal failure these measures are impracticable, and one must rely on active treatment of infection when it develops, or, at most, provide penicillin cover and barrier nursing during any temporary exacerbations of the renal failure

The treatment of established infections presents certain special features in both acute and chronic renal failure Because of the renal failure, all antibiotics are excreted at a reduced rate This is not of any great importance in the case of penicillin, but with the other more toxic substances and the sulphonamides it may lead to danger- centrations in the body To avoid this, one must ter all antibiotics, other than penicillin, in reduced doses The mode of excretion of the sulphonamides all the common antibiotics, except penicillin, is glomerular filtration, a small proportion being reab by the tubules Thus the blood level is determined entirely by the dose and by the glomerular filtratio To maintain a satisfactory level one can adjust the with reference to the glomerular filtration rate—e g, an anuric patient with no appreciable filtration would give only a single loading dose, in a person 50% of normal filtration one would give the usual l dose, and then half the normal maintenance dose, and in a person with 25% of normal filtration one w give a quarter of the normal maintenance dose, so on

For the purpose of estimating dosage of anti as indeed for all clinical purposes, the blood urea l gives an adequate indication of glomerular filtration Fig 16 shows the approximate relation of the glom filtration-rate to the blood-urea level, at different lev of protein intake, in patients in nitrogen equilibrium

Hormonal Treatment

Masson et al (1949) found that nephrectomised an survived longer than controls when they were given anabolic hormone testosterone It is therefore cc practice to administer testosterone to anuric patient doses of 5–10 mg per day The indication for the of anabolic hormones in chronic renal failure azotæmia is less strong and, so far as I know, it has been tried

Protein-sparing Diet

As Borst (1948) points out, in all patients with failure, either acute or chronic, it is wise to r katabolism by providing a diet rich in carbohydrate possibly fat. The provision of adequate non pr calories pr the brea of tissue provide ene from prote katabolis In a no person mo protein sp can be with as l as 100 g carbohydra per day (C 1947), but in patients I certain that t is insuffi and that should aim an intake 300 g or per day anuric patie this large c hydrate has additi virtues de with on p

The ance of a fat diet is so certain Th is no doubt from the of Masson et (1949), that high-fat d increases

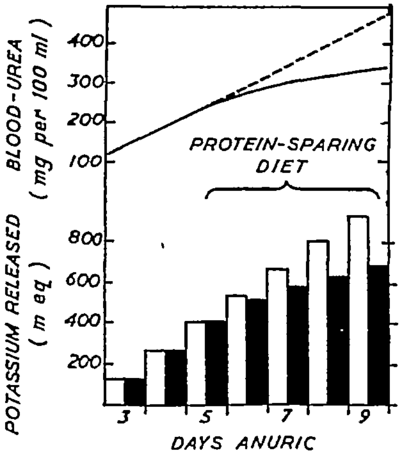

Fig 17—Effect of protein-sparing diet on rate of formation of urea and release of potassium from cells in anuria.

For the first five days of the illness the patient did not receive a protein sparing diet, and thereafter she received 2600 calories per day, as carbohydrate and fat As a result the rate of rise of the blood urea level fell By calculation from the blood urea levels and the body-weight we can estimate the quantity of potassium released from cells, here shown as a cumulative balance, each day s release being added to the previous day s total The blank histograms indicate the release that would have taken place if the patient had not received a protein sparing diet, and the solid histograms the actual quantity released Note how the protein sparing diet prevented the release of a considerable quantity of potassium urvival time of nephrectomised animals but this is robably a non specific effect of providing non protein alories Jockes, Lowe and I prescribed a high-carbo ydrate high fat diet for anuria (Bull et al 1949), but I m certain that a high-carbohydrate diet is sufficient I ave progressively reduced the fat-content of the diet nd sometimes leave it out altogether because diarrhœa levelops in some patients fed on some batches of eanut oil.

The effect of a high-carbohydrate diet in reducing atabolism in an anuric patient is shown in fig 17

ADJUSTMENT OF INTAKE

The substances whose intake it is most important to ontrol are water sodium potassium chloride and itrogen The rate of intake of these will vary according o whether the patient is in or out of normal balance or each individual substance and will also depend on he degree of impairment of renal control of excretion of each of them Thus, the regime prescribed will be in wo parts—first, correction of imbalance and secondly naintenance of balance One would always attempt to orrect the imbalances of as many substances as possible imultaneously but for convenience each substance is considered separately

Water

Underhydration —The most important abnormality of ater balance to recognise is extracellular underhydration, ith its attendant circulatory manifestations. This is sually combined with a greater or lesser degree of ellular underhydration A first approximation of the xtent of the water deficiency can be obtained clinically nd by measuring the specific gravity of the plasma y the method of Phillips et al (1950) For each 0 001 ise in the specific gravity of the plasma above 1·027 the atient lacks not less than 200 ml. of water (Phillips 1950) ome of this is extracellular water and some cellular o the appropriate ions for each compartment must ccompany the water either immediately or subse quently

It is usual to give only extracellular ions (Na Cl, and HCO$_3$) immediately and to delay the giving of intra ellular ions until later particularly potassium This is ecause an excess of intracellular ions in the extracellular pace is common in dehydration and time must be iven for them to adjust to a normal extracellular oncentration Thus, it is usually best to administer Na-containing fluids of a strength from a half to a third f the physiological This is done by administering ottles of 5% glucose between bottles of Na-containing uids The proportion of NaCl to either NaHCO$_3$ or a lactate (which is converted to NaHCO$_3$) administered ill depend on the state of acid base balance After this calculated quantity has been given a further linical assessment and an estimation of the specific ravity of the plasma should be made, and subsequent orrections ordered as necessary The volume of fluid alculated in this way may and should, be given rapidly o reduce the length of time the patient is in a state f circulatory insufficiency After the extracellular fluid olume has been corrected potassium may be given

Overhydration —Except in the anurias, the correction f overhydration is linked with that of salt retention will be considered later In anuric patients over ydration may be corrected by reducing the intake of uids to less than the insensible loss, and in some cases acupuncture Dialysis may also be used but is rarely cessary

Maintenance —The volume of fluid given will depend the ability of the kidney to excrete water and on rate of loss of fluid by routes other than the kidney ormal temperatures the rate of insensible loss of through the skin breath, and gut is about 800 ml.

A basic intake of 800 ml of fluid is therefore required in all patients In anuria, however a lower figure should be used—namely 600 ml, and not 1000 ml as Jockes, Lowe, and I prescribed previously (Bull et al. 1949) The reason for this reduction was given on p 733 —namely the production of water by the metabolism of body fat

To this basic intake should be added a volume of fluid to balance the volume of urine at optimal rates of urine flow The optimal rate of urine flow will vary with the type of renal lesion, but usually in patients with azotæmia it should be near the highest rate at which the kidney can excrete In a normal person a water diuresis causes a modest increase in rate of excretion of solutes and this persists in lesser degree in chronic renal failure Usually the greater the azotæmia the more one should attempt to achieve a high rate of urine flow, but the rate of fluid administration should never exceed the ability of the kidney to excrete water

In severely azotæmic patients (blood urea level above 100 mg per 100 ml) with chronic renal lesions, a satisfactory method of deciding on the optimal 'rate of' urine flow is to give a basic 800 ml of water, plus a volume of fluid equal to the previous day's volume of urine plus about 200 ml. The urine flow will increase and the procedure can be repeated until the urine flow is steady, or an inconveniently large intake of fluid is reached It is particularly important in these chronically azotæmic patients that the fluid intake should not fall A great many patients of this sort must have died as a result of ill advised restriction of fluids for a concentration test or for pyelography The main value of the former test is in the less severe renal lesions and I believe it should not be used in patients with a blood urea level above 100 mg per 100 ml

Sodium Intake

Correction of imbalance.—The removal of excess Na from the body is important in many conditions but I do not propose to deal with it here It is really the problem of the treatment of œdema

The correction of Na deficiency when it occurs as a part of extracellular underhydration has already been discussed, but a second type of Na deficiency without water lack, requires consideration This leads to cellular overhydration because water moves from the [illegible] cellular space to the cellular along an [illegible] (fig 5) To calculate the amount of Na necessary to correct the disturbance one may proceed as follows

Estimate the plasma Na level and subtract [illegible] *from* the normal serum Na level. This gives the deficiency in [illegible] Na per litre Superficially it seems that one would multiply the figure so obtained by the volume of the [illegible] fluid (about 15 litres) because Na is an [illegible] This quantity however is insufficient because [illegible] must be provided for the water which has moved [illegible] In practice one can assume that the deficiency [illegible] volume of distribution through total body water, [illegible] 30 litres (Black 1951) Therefore the [illegible]

(140 − x)30 m.eq of Na required, where x is the [illegible] level in m.eq per litre

Maintenance —In acute renal failure the [illegible] the maintenance dose of Na is simple [illegible] be 50–75 m.eq for each litre of urine [illegible] this figure was derived from a study [illegible] acute tubular necrosis (Bull et al [illegible]) [illegible] that the same figure is applicable in [illegible] renal failure, such as acute nephritis [illegible] and even in chronic renal lesions [illegible]

In chronic renal failure in [illegible] tion of Na is necessary [illegible] be less than 1 g per day [illegible]

In non œdematous patients [illegible] severe depletion of Na [illegible] for reasons given on p [illegible] non œdematous patients I always recommend a higher-than-normal intake of Na—200–300 m eq per day This is usually given as 3 g of $NaHCO_3$ + 2 g of NaCl, in addition to the salt ordinarily used in cooking and taken with the food If signs of œdema appear, the dose is reduced In special circumstances, particularly in the case of rarer tubular lesions without glomerular damage, different adjustments of intake may be required, and should be based on balance studies

Acid base Balance

Correction—As indicated above, a combination of clinical assessment and the determination of the plasma-HCO_3 level is usually sufficient to assess the degree of acid-base imbalance I also said that one can conveniently regard acidosis as a deficiency of base, and that this deficiency could be presumed to exist throughout total body-water Therefore, to calculate the amount of base needed to correct acidosis, one may use the formula

(27 − x)50, where x is the plasma CO_2 combining power in m eq per litre

This is best given as $NaHCO_3$ by mouth or as isotonic Na lactate intravenously

The *correction of alkalosis is slightly more complicated* in theory, but in practice the kidney can almost always make the necessary adjustments, provided the volume of extracellular fluid is normal and there is no deficiency of potassium One should therefore correct extracellular underhydration with solutions of Na chloride, and then the potassium deficiency The kidney will do the rest, even when it is severely damaged

Maintenance—In most patients with chronic renal failure there is a tendency to acidosis, because of the acid ash of most diets This should be prevented by prescribing extra alkali, usually $NaHCO_3$ For patients whose blood-urea level is above 100 mg per 100 ml I usually prescribe 2–5 g of $NaHCO_3$ per day In the rare cases of specific tubular defect much larger quantities will be required The dose may be adjusted by estimation of the plasma-HCO_3 level at intervals

Potassium

Correction of hyperpotassæmia—The particular danger of potassium retention lies in the fact that high concentrations of potassium in the extracellular fluid may cause cardiac arrest The high potassium level may be lowered either by causing the potassium to enter cells or by removing it from the body Alternatively, the toxic effect of a high potassium level may be counteracted by certain measures The most convenient method of dealing with hyperpotassæmia is to administer large quantities of glucose, which moves into the cells, taking with it potassium to form a glycogen-potassium complex This is the other reason (cf p 778) why a large intake of carbohydrate is desirable in the treatment of anuric patients The process may be hastened by simultaneous administration of insulin

Potassium may be removed from the body by dialysis, but in civilian practice it is rare for any form of dialysis to be necessary In warfare, as Meroney and Herndon (1954) have shown, the position is different Patients with gunshot wounds have large areas of necrotic muscle which release potassium at such a rate that conservative measures are not sufficiently rapid or effective Some form of dialysis is necessary, and the advantages of the artificial kidney over other forms of dialysis seem to make it the method of choice

Another less rapid method of removing potassium from the body is by feeding an ion exchange resin in the Na cycle (Evans et al 1953) The efficiency of the resin as a remover of potassium is about 1 m.eq per g in vivo in the case of the resin 'Zeo Karb 225' (Permutit Co)

It is also possible to reduce the toxic effect of hyper- mia by raising either the calcium or the Na level

Taking into consideration all these facts, Meroney Herndon (1954) describe a mixture containing calcium, and sodium which is useful for rapidly cor hyperpotassæmia

Correction of hypopotassæmia—Wherever possible is safest to administer potassium by mouth, even depleted patients Up to 10 g per day of KCl may given Where it is necessary to administer it intra-venously it may be given in concentrations of up 2 g per litre of infusion fluid, at a rate of not more 1 g per hour

It is a safe rule that potassium should never administered to anybody whose urine flow is less th 1 ml per minute

Maintenance—When the urine flow exceeds 1 ml minute, the quantities of potassium required to maint balance are not critical, except in a few circumstanc the most important of which is the early diuretic p of acute tubular necrosis Here it is best to allow urine flow to exceed 1 ml per minute for two days, allow the serum-potassium level to fall from the what high value which usually prevails in the phase Then 1–2 g of KCl per litre of urine passed be given

In rare tubular lesions and hormonal upsets b studies may be required to assess maintenance re ments for the ion

Nitrogen

The blood urea level is raised in most varieties of failure, but this in itself is of no consequence Th remains, however, the possibility that other and end-products of nitrogen metabolism are toxic, and their level rises parallel with that of urea For reason it is probably desirable to reduce the intake protein in patients with a low glomerular filtration There are, however, two other and more impo reasons for doing so

(1) Most protein foods contain potassium

(2) Urea, the most abundant end product of protein *down, accounts for a high proportion of the osmolarity* urine In most types of renal failure there is a cons osmotic diuresis (see pp 733 and 734), and this makes difficulty in maintaining water and electrolyte balance osmotic load may be reduced by diminishing the intake protein and therefore the quantity of urea to be excreted.

For these reasons a low-protein diet is desirable patients with marked azotæmia As a temporary m a protein-free diet may be given in acute renal failure in exacerbations of chronic failure, but for m in chronic failure one must always provide e protein *to take the place of the endogenous* inevitably broken down , 30 g is usually sufficient this purpose When the blood-urea level is be normal and about 70 mg per 100 ml , I usually pres a normal intake of protein of about 70 g daily the blood-urea level is between 70 mg and 120 I give about 45 g daily, and when it is above 120 the minimum of 30 g daily

Symptomatic Treatment

Anæmia—Severe degrees of anæmia should never allowed *to persist* in patients with renal failure, b they induce a mild degree of circulatory renal in ciency The hæmoglobin should be kept above 65–70 by means of blood-transfusions In certain circums (e g , in anuric patients) packed red cells should be g The usual hæmatinics, such as iron, vitamin B_{12}, f acid, and liver, have no effect on this type of an but it is said that cobaltous chloride 90–200 mg may be effective (Gardner 1953) I have no exper of this form of treatment

Vomiting—Nausea and vomiting develop in uræmic states One should first attempt to de its chemical basis—e g , cellular overhydrat

orrect it, but sometimes no obvious chemical cause can
e found Then one may use chlorpromazine (Friend
nd Cummins 1953) in doses of 25–50 mg three times
aily by injection or by mouth I have found it
oderately effective

Vomiting if persistent, makes for considerable diffi
iculties in maintaining the balance of fluids and electro
rtes. In these circumstances I have often used a
'Polythene' tube 1 0–1 5 mm in diameter passed through
he antecubital vein into the superior vena cava or
hrough the femoral vein into the inferior vena cava
hrough this tube one can administer even very concen
ated solutions such as 50% glucose by continuous
ip for long periods One man who had a severe
dominal injury, was fed thus for 56 days without
y oral intake

Stomatitis, another common complication in the gastro
estinal tract in severe renal failure is best treated
y frequent mouth washes

Diarrhœa is sometimes very troublesome and may
ove fatal Where there is a possibility that it is
luced by the diet—as sometimes happens with some
patches of peanut oil in treating anuric patients—one
ay stop oral feeding and administer the necessary
uid carbohydrate, and electrolytes intravenously In
ss severe cases I administer 1 g of streptomycin twice
aily by mouth in the hope that a change of intestinal
ora will allow the diarrhœa to settle.

Epileptiform convulsions are most often due to a
ecognisable cause—e.g hypertension and cellular over
ydration Where no cause can be found or where the
use cannot be removed barbiturates or paraldehyde
y be used in the usual dosage The same drugs may
used for restlessness insomnia and noisy delirium
t again one should seek a cause and treat it rather
n rely on symptomatic treatment

ypertension —Although not strictly a part of the
tment of uræmia the treatment of hypertension in
al failure needs to be considered here Because of
danger of further renal failure as a result of arteriolo
rosis, I usually attempt to lower hypertension in
ents with chronic renal failure when the diastolic
d pressure exceeds 110–115 mm Hg I use hexa
onium and rauwolfia serpentina for the purpose but
minister the former in particular with great caution
ne patient with severe renal failure developed a
eneralised muscular paresis which lasted nearly a week
fter a single test dose of 10 mg of hexamethonium
now usually start with a dose of 1 mg

Conclusions

I have tried to show that renal failure gives rise to
ny clinical pictures—the uræmias. These uræmias are
t an inevitable consequence of renal failure but result
m imbalance between the rate of loss and the rate of
ake or of production in the body of certain chemical
stances. Some at least can be prevented by adjustment
f the diet

REFERENCES

kel H., Smallwood W C Smellie J M, Hickmans E M
(1953) *Acta pædiat Stockh* 42 suppl 90 27
ck D A K (1951) *Brit med J* ii 1407
nt J G G (1948) *Lancet* i, 891
wn M R Currens J H Marchand J F (1944) *J Amer med
Ass.* 124, 545
l, G M Joekes, A M, Lowe, K G (1949) *Lancet* ii 229
— — (1950) *Clin Sci* 9 379
ach L (191) *Im r J Roentgenol* 58 6 0
s H M Hughes J nes \ C Milne M D Yellowlees H
(1953) *Lancet* ii 791
Milne M D (1954) *Brit med J* ii 1007
erg A M (1939) Hypertension and Nephritis 4th ed.,
milton
nt Smith, F Fremont Smith M, Dailey M E, Solomon P
etten D Carroll M I (1951) *J clin Invest* 9 1
l D G Cummins J F (1953) *J Amer med Ass* 153 180
Brentano J L (1953) Thèse de Paris
e J L (1917) *Harvey Lect* 42 247.
r F H (1953) *J Lab clin Med* 41 56.

References continued at foot of next column

CHLORPROMAZINE IN OBSESSIVE-COMPULSIVE AND ALLIED DISORDERS

W H TRETHOWAN
M.B Camb M R C.P D P.M
SENIOR LECTURER IN PSYCHIATRY IN THE UNIVERSITY OF
MANCHESTER

P A. L SCOTT
M B B.Sc St And D.P M
PSYCHIATRIC REGISTRAR, MANCHESTER ROYAL INFIRMARY

REPORTS of the psychiatric use of chlorpromazine in patients are now fairly numerous Favourable claims chiefly of the control of agitation and excitement in patients with various psychoses, came initially from the Continent (Hamon et al. 1952 Delay and Deniker 1952 Delay et al 1953 Arnold et al 1953, Deschamps and Cadoret 1953) At Basle in November, 1953, 893 cases so treated were discussed (Staehelin 1954) these included cases of depression (Kielholz 1954) and a considerable number of schizophrenics (Labhardt 1954) in many of whom substantial improvement was reported.

From England the number of reports has been less. The findings (Anton Stephens 1954 Garmany et al 1954 Lancaster and Jones 1954 Elkes and Elkes 1954) though favourable are less conclusive than those of the Continental workers

Although chlorpromazine is valuable in the treatment of severer forms of mental disorder among inpatients its efficacy in the treatment of outpatients with less overt mental disturbances is not so well established Garmany et al (1954) who investigated the effects of chlorpromazine in 29 psychoneurotic patients found that all patients in whom tension was prominent improved but they could not confirm the relief from obsessional symptoms claimed by Sigwald and Bouttier (1953)

However, since patients with intractable obsessive-compulsive symptoms form a substantial proportion of those attending psychiatric outpatient clinics and demand much time and attention any possibility of obtaining some relief in these cases should be explored. This was the main purpose of the present investigation

In addition the impression has been gained that chlorpromazine is at present fairly widely used not only in psychiatric clinics and hospitals but also by general practitioners The fact that this treatment is not apparently devoid of risk argues the need for a clearer understanding of its effects and the indications for its use

Clinical Material

75 outpatients (36 men and 39 women) were originally selected for a therapeutic trial of chlorpromazine Owing to irregular attendance (5 cases) intercurrent physical illness (6 cases) and complications arising from the treatment (5 cases) 16 patients did not complete a

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PROF BULL REFERENCES—*continued*

Hamburger J Mathé G (1954) Ciba Symposium The Kidney London
— — Crosnier, J (1950) *Bull Soc méd Hôp Paris* 66 1716.
Masson, G M C, Corcoran A C Page I H (1949) *J Lab clin. Med.* 34 925
Meroney, W H., Herndon, R F (1954) *J Amer med. Ass* 155 877
Merrill, J P (1953) Personal communication.
Mudge G H. (1951) *Amer J Physiol.* 165, 113
Nickel J F, Lowrance, P B Leifer E, Bradley S. E (1953) *J clin Invest* 32, 68
Orloff J Kennedy T J jun. Berliner, R. W (1953) *Ibid* p 538
Phillips, R A (1950) Personal communication.
— Van Slyke D D Hamilton, P B Dole V P., Emerson, K Archibald R. M (1950) *J biol Chem.* 183 305.
Piorry P A Lhéritier D (1840) Traité des altérations du sang Paris Cited by Fishberg (1939)
Platt R. (1950) *Clin Sci* 9 367
Rapoport, S., Brodsky W A., West C. D Mackler B (1949) *Amer J Physiol* 156 433
Robinson, J R. (1953) *Biol Rev* 28 158
Smith H. W (1951) The Kidney: Structure and Function in Health and Disease New York.
Thorn, G W Koepf, G F., Clinton, M jun. (1944) *New Engl. J Med* 231 76

TABLE I—PRINCIPAL SYMPTOMS COMPLAINED OF *

Symptom	No of cases		
	Moderate	Severe	Total
Mental			
Anxiety and tension	16	38	54 (*91%*)
Irritability	35	14	49 (*83%*)
Hypochondriacal symptoms	19	26	45 (*76%*)
Excessive self-criticism	23	20	43 (*73%*)
Indecision	24	17	41 (*69%*)
Depression	23	16	39 (*66%*)
Self-consciousness	18	18	36 (*61%*)
Lack of concentration	22	12	34 (*58%*)
Phobias	10	21	31 (*53%*)
Compulsive rituals	8	11	19 (*32%*)
Aggressive urges towards self or others	6	13	19 (*32%*)
Insomnia	8	9	17 (*29%*)
Intellectual rumination	6	7	13 (*22%*)
Ego disorder (unreality feelings, &c)	8	2	10 (*17%*)
Somatic or autonomic			
Sweating	19	8	27 (*46%*)
Headaches	17	7	24 (*41%*)
Trembling	18	5	23 (*39%*)
Palpitations	15	7	22 (*38%*)
Aches and pains	10	10	20 (*34%*)
Loss of appetite	11	8	19 (*32%*)
Digestive disturbances	7	8	15 (*25%*)
Stammer	1		1
Tinnitus		1	1
Ejaculatio		1	1
Writer's cramp		1	1

* Mild episodic symptoms are excluded

course of sufficient length or regularity to permit valid conclusions to be drawn Further reference to some of these will be made when side effects are discussed The clinical assessment of the results is therefore confined to 59 patients (30 men and 29 women)

Only those who had psychoneuroses or personality disorders with some symptoms of an obsessive or compulsive kind were selected

Age—The patients were aged 20–57 (average 35), 32 (54%) were aged 25–35

Duration of symptoms—In only 11 patients (18%) was the total duration of symptoms relatively short—from 4 months to 4 years In 18 (30%) nervous symptoms had been present, either continuously or with occasional remissions, ever since childhood In another 9 (15%) symptoms appeared during adolescence (i e, at the age of 12–15) and persisted from that time In the remaining 21 patients (36%), whose illness did not begin until after the age of 18, this was also of long duration (up to 26 years), with periodic variations in intensity

Diagnosis and classification—Diagnostic subdivision of cases of this kind is at present somewhat controversial In view of this more attention was paid, in comparing the patients, to the presence, absence, severity, and persistence of symptoms than to formal diagnosis (table I) However, some arbitrary divisions are possible 6 patients only exhibited the classical obsessive compulsive neurosis, 11 had symptoms predominantly of a phobic kind (e g, fear of crowds and of going out alone), 11 others were constantly preoccupied with morbid thoughts or impulses (e g, aggressive urges towards self or others and obsessions of jealousy), and in 13 the presenting picture was mainly hypochondriacal The remainder showed mixed clinical conditions, usually states of tension, irritability, anxiety, and secondary depression coloured by obsessive-compulsive features and accompanied by somatic complaints, though almost every known variant was present, including hysterical features in 5 cases

Degree of disability—This was assessed both before and after treatment by the use of an 11 point scale, positioning on which depended not only on the number and severity of symptoms but also on each patient's estimated working capacity and effectiveness as a social ble II) Initially 35 patients (59%) were placed th and 5th points of the scale and thus could be considered as moderately incapacitated by symp The positioning of the remainder appeared to follo normal distribution around this peak.

Method of Investigation

(1) The patients were observed for 7–18 weeks—in two thirds of the cases for 12–14 weeks All patients attended weekly for 7–15 weeks, after wh some were seen at intervals of 2, 3, or 4 weeks

(2) All the patients received both chlorpromazine an inert, though apparently identical, placebo, b being taken by mouth No patient knew which being given or that a placebo was being used at all.

(3) In addition more than half the patients had a without treatment at some time during the course.

(4) The course of treatment was controlled by investigator only The other remained ignorant only of what was being given but also of alterations dosage

(5) 31 patients began treatment with ch and 28 with the placebo This was determined by cha (odd or even number of letters in surname) the course of treatment was to plan, modified in a cases by individual response

(6) During the initial period (7–18 weeks) four dif courses of treatment were used

(*a*) Chlorpromazine for 4–5 weeks, placebo for 1–3 w *and chlorpromazine for 2–13 weeks (14 patients)*

(*b*) Chlorpromazine for 4–6 weeks, placebo for 1–2 and no treatment for 1 week (17 patients)

(*c*) Placebo for 2–3 weeks, chlorpromazine for 4–6 and placebo for 1–3 weeks (13 patients)

(*d*) Placebo for 2–3 weeks, chlorpromazine for 4–7 and no treatment for 1 week (15 patients)

(7) After the initial period 42 patients received fur treatment with chlorpromazine alone (29 cases) or both chlorpromazine and placebo alternately (12 or with placebo alone (1 case)

(8) Initially chlorpromazine 50–75 mg was pres daily The daily dose was increased in the second to 100 mg and in the third and subsequent week 150 or 200 mg, at which level it was maintained

(9) *At every visit all the patients were seen se* by each observer, both of whom made an indepen

TABLE II—CLINICAL RATING SCALE OF DEGREE OF DIS

	No of patie	
	Before treatment	*Af tr*
(1) Ill enough to need hospital admission	0	3
(2) *Intermediate between 1 and 3**	0	1
(3) Severely incapacitated—e g unable to work/perform domestic duties unable to go out unaccompanied fully preoccupied with obsessions, compulsive rituals phobias, &c severe continuous tension, anxiety or depression	2	3
(4) Intermediate	8	6
(5) Moderately incapacitated—e g working irregularly or continuously with difficulty domestically and socially ineffective variably severely preoccupied with obsessions &c moderate continuous/severe episodic tension anxiety or depression	18	7
(6) Intermediate	17	7
(7) Mildly incapacitated—e g able to work/do domestic duties social activity not completely satisfactory obsessions &c, only occasionally prominent mild continuous/moderate episodic tension anxiety or depression	10	1
(8) Intermediate	4	11
(9) Slight incapacity only—e g able to work with some efficiency no impairment of social or domestic life obsessions, &c though episodically present largely in background mild episodic tension, anxiety or depression	0	5
(10) Intermediate	0	3
(11) No apparent disability whatsoever	0	1

* Those placed in intermediate categories either varied bet showed some features of, both neighbouring groups

assessment one using the method of the ordinary psychiatric interview, the other a questionnaire devised to record and compare statistically the changes in number and severity of each patient's main symptoms

(10) The weight and blood pressure of every patient were recorded at each attendance

Results

A significant response to chlorpromazine compared with the response to the placebo was observed in 27 (46%) patients In the other 32 (54%) there was no significant difference in the responses to chlorpromazine and to the placebo, though in some cases changes in condition took place (table III)

Responses to Chlorpromazine

27 patients responded to the first course of chlorpromazine 14 of them began treatment with the acebo for 2 weeks, during which there was no appreciable change In 2 other patients this period was extended 3 weeks because of a slight transient initial improvement, presumably due to suggestion, which disappeared by the end of the 3rd week After this all 14 were treated with chlorpromazine The remaining 13 patients were given chlorpromazine from the start

After 4–6 weeks on chlorpromazine 21 patients were given the placebo again while the remaining 6 patients were left without treatment for a week.

All 27 patients had a return of symptoms usually within 3–5 days of withdrawal of the chlorpromazine The severity of the relapse varied the condition of most patients returning to the pre treatment level 6 patients however became considerably worse than before 3 of these developed a state of agitated depression of such severity that admission to hospital became necessary

Although after relapse all 27 patients were again given chlorpromazine 10 now did not respond and in the remaining 17 the response was on the whole less satisfactory than that originally observed Although the 6 patients who relapsed most severely were all among those who originally responded best, only 2 showed any response to the second course of chlorpromazine in 1 one was the response as good as before in the other it was slight In the remaining 4 patients the exacerbation of symptoms persisted unchanged

TABLE III—RESPONSES TO CHLORPROMAZINE

	Men	Women	Total	
Positive response to chlorpromazine compared with response to placebo.				
(a) Response to 1st course of chlorpromazine with relapse when this was withdrawn				
Moderate to good response	10	9	19	
Slight response only	4	4	8	
Total	14	13	27	(46%)
(b) Response to 2nd course of chlorpromazine in those responding to 1st course and relapsing after this was withdrawn				
Moderate to good response	5	6	11	
Slight response only	2	4	6	
Total	7	10	17	(29%)
(c) Non responsive to 2nd course following relapse after withdrawal of 1st course	7	3	10	(17%)
Negative response to 1st or subsequent course of chlorpromazine compared with response to placebo				
(a) Equal improvement with chlorpromazine and placebo with no relapse when chlorpromazine was withdrawn:				
Moderate to good improvement	4	2	6	
Slight improvement only	3	1	4	
Total	7	3	10	(17%)
(b) No essential change on either chlorpromazine or placebo	9	11	20	(34%)
(c) Worse		2	2	(3%)
Total	16	16	32	(54%)

TABLE IV—CHANGES IN CLINICAL CONDITION OF ALL PATIENTS AT END COMPARED WITH BEGINNING OF INVESTIGATION AND TREATMENT

Change	No of points gained or lost on rating scale	Men	Women	Total	
Improved					
Good	+5	1		1	
	+4	3	1	4	
Moderate	+3	2	4	6	
	+2	3	3	6	
Slight	+1	5	5	10	
Total		14	13	27	(46%)
None	0	8	12	*20	(34%)
Worse					
Slightly	−1	3	2	5	
Moderately	−2	3	2	5	
	−3	1		1	
Much worse	−4	1		1	
Total		8	4	12	(20%)

* See table II

No Response to Chlorpromazine

32 patients showed no response to chlorpromazine The condition of 20 remained essentially unchanged throughout that of 2 others became rather worse

In 10 patients some improvement took place, in 6 to a considerable degree None of these patients relapsed when chlorpromazine was withdrawn or when the placebo was again substituted all maintaining their improvement whatever plan of treatment was followed Although there was no initial change in the condition of 3 of these patients who started treatment with two weeks on the placebo the improvement later observed both in these and in the 7 other patients who were put on chlorpromazine from the start could not be definitely ascribed to the chlorpromazine but was more probably due either to spontaneous remission or to suggestion

The final condition of all the patients at the end, compared with the beginning of the investigation is summarised in table IV

Response of Individual Symptoms

(1) The following symptoms showed the most response to chlorpromazine compared with the response to placebo (differences significant at $p=0{\cdot}02$ or higher): loss of appetite anxiety and tension, irritability hypochondriacal symptoms aggressive urges towards self or others, lack of concentration and difficulty in getting to sleep

(2) Symptoms which responded to some extent to chlorpromazine but not significantly so compared with the response to placebo were palpitations, sweating, aches and pains trembling phobias indecision intellectual rumination self-consciousness depression, ego disorders, waking at night, excessive self-criticism, stammer and tinnitus

(3) The following symptoms showed no response to chlorpromazine compared with that to placebo: headaches digestive disturbances, compulsive rituals, writer's cramp and facial tic

(4) Symptoms which became significantly worse when the placebo was substituted for chlorpromazine, compared with the period on placebo preceding the first course of chlorpromazine, were anxiety and tension, depression palpitations and sweating

Changes in Weight

47 patients (80%) gained weight during treatment—up to $16^1/_4$ lb In 2 patients the weight remained stationary while 9 lost up to $6^3/_4$ lb 1 other obese overweight patient lost $11^1/_4$ lb The average weight change of the whole group was +4 lb

Though there was no clear relationship between gain in weight and degree of clinical improvement those whose symptoms responded to chlorpromazine gained

TABLE V—COMPLICATIONS AND SIDE EFFECTS

	No of patients	*Approx proportion (%) of total*
Drowsiness	35	50
Transient or postural dizziness	9	13
Vivid dreams or nightmares	8	11 5
Skin rashes	7	10
Constipation	7	10
Pyrexial attacks	6	8 5
Thirst or dryness of mouth	5	7
Abdominal discomfort	3	4
Jaundice	3	4
Hypnagogic hallucinations	2	3
No definite side effects	13	19

* The incidence of side-effects is assessed in relation to 70 of the original 75 patients The other 5 did not attend for more than two consecutive weeks and received placebo only

more (average $4^1/_2$ lb) than in those who showed no positive response (average $2^3/_4$ lb)

Blood pressure

In 55 patients (93%) a transient fall in systolic blood-pressure, up to 60 mm Hg (average 19 mm Hg), took [illegible] under treatment with chlorpromazine A fall in [illegible] pressure, up to 30 mm Hg (average 19 mm Hg), was observed in 45 patients (76%) The remaining patients showed some variations but little change in relation to treatment The blood-pressure of most patients though somewhat lower at the end, compared [illegible] the beginning, of the investigation was not significantly so

Complications and Side effects (table v)

Jaundice, the most serious complication, developed in [illegible] patients (1 woman and 2 men) after 9, 18, and 19 days' treatment, during which about 1075, 2200, and 2450 mg of chlorpromazine had been given In all 3 the attack [illegible] 2–3 weeks and clinically resembled a mild attack of infective hepatitis None had had a previous attack of jaundice, though this was recorded in the history of [illegible] of the 70 patients

Skin rashes, although observed in 7 patients, did not constitute a serious bar to further treatment Treatment was stopped in 1 case largely because the patient found that she was pregnant, which seemed to promote a spontaneous remission of symptoms The rashes were of various types, erythematous, maculopapular, and urticarial, preceded and accompanied by itching The distribution was usually widespread, the neck, upper arms, shoulders, chest, and thighs being mainly affected One patient, a sufferer from ichthyosis, developed an outbreak of eczema on the fingers Either reduction of dosage or temporary cessation of treatment effected a speedy resolution of all these skin reactions

At least 6 patients developed *pyrexia* during treatment It usually lasted 48 hours, the main symptoms being sweating, severe headache, nausea, epigastric discomfort, and aching in the limbs and back The number may have been higher, but, since the attacks were not actually observed but described retrospectively by the patients at their weekly visits, and because of a concurrent widespread outbreak of upper respiratory infection, the symptoms proved difficult to assess Rhinitis, sore throat, and other indications of upper respiratory infection were, however, absent in these cases In addition 2 patients described vivid hypnagogic hallucinations in association with the attack In all cases treatment was continued without prolongation of the symptoms.

Other *minor side effects* complained of included transient or postural dizziness probably related to a fall or to increased lability of blood-pressure, thirst, abdominal discomfort, and constipation 8 patients commented spontaneously on the occurrence of vivid dreams or nightmares Some drowsiness developed initially in at least half the patients, and recurred in some cases when the dosage was raised, but in either event passed off [illegible] within a few days 1 patient, however, com[illegible] severe drowsiness and discontinued attendance [illegible] reason

Discussion

Although from the therapeutic point of view the results of the present investigation are not impres they might have been better if a different plan of tr ment had been used 27 of the patients appeared receive some benefit from chlorpromazine in the stages, but only 19 of these improved to any degree

The return of symptoms after sudden withdrawal chlorpromazine in all these cases, but not in the 10 patients who appeared to improve spontaneously, ag closely with the findings of Azima and Ogle (1954), observed similar relapses in 70% of their patients

Moreover, after the withdrawal of chlorpro there was significantly less response to a further co In view of this and the fact that the condition of patients in relapse was more severe than their o condition, it cannot be overemphasised that, where satisfactory response appears to be produced, trea should not be precipitately withdrawn but should be tinued with, perhaps, a gradual reduction of dosage la

The *occurrence of jaundice in 3 of 70* patients closely with the recorded incidence of some investigators (Azima and Ogle 1954, Elkes and 1954, Lancaster and Jones 1954) and almost exac with that of Lehmann and Hanrahan (1954), observed this complication in 3 of 71 cases The c needs further elucidation, but since 1 of the patients had been in close contact with a case of infe hepatitis 6–8 weeks earlier, it is of interest that A and Ogle, who observed this complication in 5 of cases, recorded a concurrence of infective hepatitis the community The fact that jaundice developed all 3 cases within a short time, after a relatively s dosage had been given, suggests either idiosyncrasy some other predisposition

Apart from jaundice, which indicates a need caution in the use of chlorpromazine, other side-effe are common and may be unpleasant

The incidence of pyrexia was lower in the present seri than in the 10% of patients treated by Garmany et (1954), but a possible reason for this has been indicat The *development of hypnagogic hallucinations* in patients is believed to be a new observation, but An Stephens (1954) has already remarked that dreams increase

Despite difficulties chlorpromazine is clearly of v in the treatment of neurotic disorders in which and tension are prominent, this was also the opinion Garmany and other workers Furthermore it appe that chlorpromazine may safely be used to treat patients, providing adequate supervision is ma and the patients are instructed to report immedia any unusual symptoms Although a previous history jaundice, unless recent, is not necessarily a co indication, it seems unwise to give chlorpromazine patients suspected of hepatic dysfunction

Compared with the widely used combination of d amphetamine and amylobarbitone, which, alth merely a euphoriant, has the advantage of being free from side effects, chlorpromazine appears to rather more effective and specific in controlling sym of anxiety and tension, in addition it produces increase in appetite and weight.

In the control of classical obsessive comp symptoms chlorpromazine has proved disap Though some phobic symptoms and intellectual tion seemed to be partially relieved, no lessening of incidence and severity of compulsive rituals was ob The only compulsive symptoms responding signific to chlorpromazine were aggressive urges towards self others and obsessive hypochondriacal ideas

In the selection of patients for treatment with ch promazine the presence of anxiety, tension, and ce ther symptoms provides a more reliable criterion than oes the degree of conformity with any theoretical or ebatable diagnostic category

Summary

The effects of chlorpromazine on 59 outpatients suf ring from neurotic disorders with obsessive-compulsive atures were investigated

All the patients received, at different times both hlorpromazine and an apparently identical inert placebo

In those who responded sudden withdrawal of chlor romazine produced a relapse. After this some did not espond when chlorpromazine was again given The nadvisability of sudden withdrawal is emphasised

Those patients in whom tension and anxiety were rominent did best Little relief of obsessive-compulsive ymptoms apart from aggressive urges and hypo hondriacal ideas was obtained

The frequency of side-effects was assessed in 70 atients Although common none were serious except aundice which occurred in 3 cases

We wish to thank Prof E W Anderson for his advice and ssistance

REFERENCES

nton-Stephens, D (1954) *J ment Sci* 100 513
rnold, O H Hift S., Solms, W (1953) *Wien. med Wschr* 103, 503
ama H Ogle W (1954) *Canad med Ass J* 71, 116
elay J Deniker, P (1952) Congrès des médecins aliénistes et neurologistes de France et des pays de langue française. Luxembourg
— — Tardieu, Y (1953) *Pr méd* 61 1166
eschamps, A Cadoret, M. (1953) *Ibid* p 878.
lkes J Elkes, C (1954) *Brit med J* ii, 560
armany, G May A R., Folkson, A. (1954) *Ibid* p 439
Hamon J., Paraire J Velluz, J (1952) *Ann. méd psychol* 110 331
ielholz, P (1954) *Schweiz Arch. Neurol Psychiat* 73 291 431
abhardt, F (1954) *Ibid* p 309
ancaster N P Jones, D H. (1954) *Brit med. J* ii 505
ehmann H E Hanrahan G E. (1954) *Arch Neurol. Psychiat.* 71, 227
igwald J, Bouttier, D (1953) *Ann. Méd.* 54 150 *Pr méd* 61, 607
taehelin J E. (1954) *Schweiz. Arch Neurol. Psychiat* 73 288

RADIOLOGY IN THE MANAGEMENT OF ANTERIOR PLACENTA PRÆVIA

J K RUSSELL
M.D Aberd M.R C O G
LECTURER IN OBSTETRICS AND GYNÆCOLOGY,
UNIVERSITY OF DURHAM

C K WARRICK
M.B Lond. F R C.S.E., F.F.R
ASSISTANT RADIOLOGIST ROYAL VICTORIA INFIRMARY
NEWCASTLE UPON TYNE

rom King's College Durham University and the Princess Mary Maternity Hospital Newcastle upon Tyne

As a result of the renewed interest in radiological ocalisation of the placental site for which the work of Reid (1949 1951 1952) was principally responsible it is ow widely appreciated that radiology has brought a new ccuracy to the diagnosis of placenta prævia

Techniques have been described by Whitehead (1953) and Iartley (1954) and modifications of these and other methods re in use in many centres. Stallworthy (1951) and Dawson nd Mitchell (1954) have described the clinical application of adiology in cases of antepartum hæmorrhage and it has een shown that many patients who would otherwise have ad to spend weeks in hospital can now be discharged safely their homes In other cases placenta prævia has been orrectly diagnosed before any bleeding.

We draw attention here to the precision which radiology an give to the management of anterior placenta prævia he point is illustrated in the following two case reports

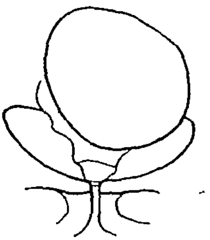

Fig. 1

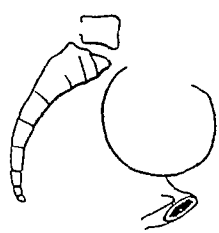

Fig. 2.

Fig 1—Case 1 : anteroposterior position showing displacement of fœtal head to the left.

Fig 2—Case 1 : lateral erect position showing 2 cm. separation of fœtal head from pubis.

Case reports

Case 1 —A woman was admitted to the Princess Mary aternity Hospital as an emergency case on July 25 1953 when 30 weeks pregnant a brisk vaginal hæmorrhage had taken place a few hours before admission.

On admission the patient's general condition was satisfactory and she was kept at rest in bed for a week after which a radiological examination was made (figs. 1 and 2)

Radiologist's Report (Aug 1 1953) — Single fœtus cephalic presentation Occiput to the left The head is not engaged and is placed asymmetrically in relation to the pelvic inlet in the anteroposterior film In the lateral projection the head is separated from the sacral promontory by 1 0 cm and from the symphysis pubis by 2·0 cm.* These measurements, combined with the displacement of the fœtal head in the anteroposterior film and the situation of the soft-tissue shadow indicate the presence of right anterior placenta prævia.'

Subsequent History—Four days after this report was received arrangements were made for the patient to be examined in the theatre and the pædiatrician was warned that if a cæsarean section proved necessary the placenta might be damaged in the course of the operation and the baby require transfusion. Vaginal examination revealed that the internal cervical os was covered by placental tissue, and an immediate lower segment cæsarean section was done The placenta as expected, was found under the uterine incision. Guided by the radiologist's report that the placenta was lying mainly to the right the operator passed his hand towards the left side separating the placenta from the uterine wall and was able to circumvent it without undue difficulty The baby was delivered and the cord clamped without delay Although the placental substance was disrupted no fœtal vessel was damaged. The baby made excellent progress.

Case 2 —A primigravida aged 31 was admitted to the Princess Mary Maternity Hospital as an emergency case of antepartum hæmorrhage on May 4 1954 She had been married for 10 years and had never taken precautions against pregnancy She was 34 weeks pregnant on admission, and the clinical features suggested placenta prævia. She was examined radiologically on May 17, 1954 (figs 3 and 4)

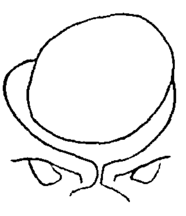

Fig 3

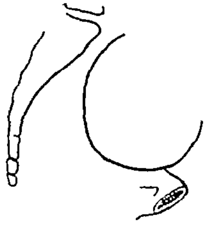

Fig. 4.

Fig 3—Case 2 : semi-erect anteroposterior position showing slight displacement of fœtal head to the left.

Fig 4—Case 2 : lateral erect position showing 2 cm. separation of fœtal head from pubis.

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* All radiological measurements have been corrected for magnification.

Radiologist's Report — "Single fœtus, cephalic presentation, occiput to right side The uterine shadow is thickened anteriorly The fœtal head is separated by 1 5 cm from the sacral promontory and 2 0 cm from the symphysis pubis There is slight asymmetry in the semi erect anteroposterior radiograph The appearances indicate the presence of right anterior placenta prævia "

Subsequent History —The patient remained in hospital, and small vaginal hæmorrhages occurred on two or three occasions At the 38th week the patient was examined in the theatre, and the pædiatrician was warned about the possibility of placental damage at operation The placental edge was felt anteriorly 3/4 inch from the cervical os, the examination caused a brief hæmorrhage, and in view of the long period of infertility it was decided to do a cæsarean section The placenta covered the anterior wall of the lower uterine segment, but in view of the radiologist's report the operator was again able to circumvent the placenta without difficulty The placenta was partially disrupted, but no fœtal vessel was pierced The baby made excellent progress

Discussion

When the placenta is situated anteriorly in the lower uterine segment, cæsarean section carries a particular risk for the fœtus, blood loss from the fœtal circulation, the result of laceration of the placenta, may place the life of the child in jeopardy The extent of this hazard and the manner in which it might best be handled were studied carefully in the Princess Mary Maternity Hospital by Neligan and Russell (1954) Between January, 1951, and March, 1953, 45 lower-segment cæsarean sections were done for placenta prævia, and the placenta was found in the incision 20 times, in 11 instances there was significant damage to the fœtal circulation, and 7 babies were transfused This injury was the direct cause of 1 neonatal death

For the past two years the obstetric staff of the hospital have paid special attention to operative technique in these cases During this period 35 cæsarean sections have been done for placenta prævia, the placenta was found in the uterine incision in 15 of the cases In no instance has there been significant damage to the fœtal circulation, and none of the babies has required transfusion

In some measure the improvement in results has been due to the increased use in the hospital of radiological localisation of the placenta In 5 of the 15 cases with an anterior placenta prævia the obstetric staff were forewarned of its site by the radiologist, details of 2 cases have been given above When a severe degree of anterior placenta prævia is noted by the radiologist, we ensure that the case is managed personally by a senior member of the staff thoroughly conversant with the operative technique required to avoid damaging the placenta Our pædiatric colleagues are also advised about the possibility of damage to the fœtal circulation In the 2 cases reported above the operator received valuable information from the radiologist about the best way of circumventing the placenta without damaging fœtal vessels

In our experience radiology is making a significant contribution to the management of this important type of placenta prævia

Summary

Localisation of the placenta by radiography is now used in many centres in this country, but the extent of the contribution which the method can make to the management of placenta prævia has yet to be determined

When the placenta is situated anteriorly, there is an increased risk of damage to the fœtal circulation in cases of cæsarean section In the Princess Mary Maternity Hospital radiology is adding a new precision to the management of this important type of placenta prævia

We are grateful to Prof Harvey Evers for permission to details of cases admitted to the Princess Mary Hospital under his care The tracings of the radiographs were made by the department of pho of the University of Durham

REFERENCES

Dawson, J, Mitchell, P R (1954) *Brit med J* ii, 1085
Hartley, J B (1954) *Brit J Radiol* 27 365
Neligan, G A, Russell, J K (1954) *J Obstet Gynæc., Brit E*
61, 206
Reid, F (1949) *Brit J Radiol* 22 81
— (1951) *Proc R Soc Med* 44, 703
— (1952) *Postgrad med J* 28, 445
Stallworthy, J (1951) *Amer J Obstet Gynec* 61, 720
Whitehead, A S (1953) *J Fac Radiol, Lond* 4 245

BRONCHIAL CARCINOMA

SURVEY OF 317 PATIENTS

J R BIGNALL
M.A, M D Camb, M R C P

SENIOR LECTURER, INSTITUTE OF DISEASES OF THE
BROMPTON HOSPITAL, RESEARCH ASSISTANT, INSTITUTE
CANCER RESEARCH, ROYAL MARSDEN HOSPITAL

THE Brompton Hospital and the Royal M Hospital are specialised hospitals, the former is cerned with diseases of the chest and the latter with types of cancer Both draw their patients predomin from London and the southern counties, but ne serves a particular area Many patients are first elsewhere and are sent for bronchoscopy, surgical ment, radiotherapy, or a second opinion Some directly from their general practitioner, and a few abroad The story of the patients with bro carcinoma at these hospitals does not therefore pr the experience of all such patients throughout country

The hospitals are linked by a joint consultative cl for the study of the disease, and in particular its treat ment by radiotherapy (Brooks et al 1951) D 1951, 317 patients with bronchial carcinoma atter the hospitals All but 1 have been followed for two ye from their first attendance 1 patient left the co soon after radiotherapy and is considered to have d This report describes the history of these patients, far as it has been discovered by observation at joint consultative clinic, and from hospital records reports from general practitioners

Validity of the Diagnosis

The diagnosis was based on histological evidence 199 (62%) of the 317 cases The tissue was obta by bronchial biopsy in 91, removal of the tumour 53 and of a metastasis in 27, necropsy in 16, of sputum in 11, and drill biopsy in 1

There was no histological confirmation in 118 (cases In 10 cases there was macroscopic evidence necropsy but no further examination was made patients were found to have inoperable tumours thoracotomy There was clinical or radiographic evi of metastases in 48, and bronchoscopic evidence of tumour in 13 and of mediastinal metastases in In 20 there were other suggestive broncho abnormalities although no tumour was seen In 8 (2 5%), therefore, did the diagnosis rest purely clinical and radiographic evidence of pulmon abnormalities

Certain diagnosis is difficult Even at necropsy diagnosis without histological examination may wrong, there are 2 examples of this event in the rec of the joint consultative clinic (Smithers 1953) It se reasonably probable, however, that all but a very of the 317 patients did have a bronchial carcinoma

Composition of the Group

The group contained a high proportion of pa between 50 and 60 years of age and a low pr ver 70 The age distribution of patients with bronchial arcinoma throughout the population is not known stimates based on death certificates are probably inaccurate owing to the difficulty of diagnosis without investigation in hospital. It is likely that fewer old eople will be fully investigated; and the proportion ver 70 may therefore be falsified by wrong diagnoses Death certificates during 1951 showed that 20% of the 3 247 recorded cases were in patients over 70 (Registrar General 1951) Hospital necropsy records may be no more accurate, for cases are selected both for admission o the particular hospitals and for examination after eath A series of 741 necropsies in several London hospitals during 1948–52 contained 16% over 70 Galuzzi and Payne 1955) The proportion of the present group over 70 (5%) is considerably lower than either of the other estimates This is not unexpected at two pecial hospitals with full facilities for surgical treatment and radiotherapy

There was also a very low proportion of women over 70 (6%) compared with the proportions in the necropsy and death-certificate records (24%) The numbers involved are very small During 1952 slightly more patients with bronchial carcinoma were seen The proportion of those between 50 and 60 was lower and over 70 higher, than in the previous year There was also a higher proportion of older women However the proportion in the two years combined is still much lower than the estimate from death certificates and necropsies

The frequency of the main histological types differs from that in necropsy reports Necropsy estimates cannot be accepted as the true distribution for they may well be biased in favour of the more malignant growths hose causing death before diagnosis or producing a rapidly fatal illness. On the other hand estimates from hospital records may contain too few malignant tumours. Histological examination is less likely in patients who already have extrathoracic metastases or are clearly beyond hope of effective treatment Certainly the frequency of overt metastases when the patients first attended hospital was twice as great in the present series in those without histological confirmation (40%) as in those with it (20%) Both hospital and necropsy records suggest that the proportion of undifferentiated tumours is a little greater in women than in men. In the present series there were ten times as many men as women whereas the ratio in 1951 according to death certificates was approximately 5 to 1 Registrar-General 1951) In necropsy records (Bryson and Spencer 1951 Galuzzi and Payne 1955) undifferentiated tumours make up about two thirds of the total and squamous tumours a fifth but in the present group and in a larger one also drawn mainly from special hospitals (Doll and Hill 1952) undifferentiated tumours were reported in only a little over a third and squamous in approximately a half of the patients in whom the type was known It is impossible to find out how much the pattern of histological types in the whole group differs from that of the sample examined or whether estimates from hospital records are closer to the real frequency than those from necropsies Such comparisons of histological types are very uncertain for classification of the tumours depends on the particular portion examined as well as on the pathologist's interpretation of the appearances In the present series, for instance lthough the same pathologist reported on almost all the sections the type reported from the bronchial biopsy differed from that reported from the whole tumour or a metastasis in 9 of the 114 cases in which both examinations were done

It seems reasonable to conclude that the present series compared with all patients with lung cancer ontains fewer with undifferentiated tumours as well s fewer women and old people

History Before Going to Hospital

It is often difficult for the patient to remember when his symptoms began, particularly when the first indication of ill health was merely an unaccustomed tiredness, shortness of breath, or change in a long-standing cough

The estimate of duration of illness is, therefore frequently only very approximate In the few patients who had no symptoms at all the illness is considered to have begun at the time the radiographic abnormalities were found Owing to the method by which the patients were referred to the hospitals a long history of symptoms at the first attendance does not necessarily indicate delay in diagnosis

A little over a fifth had had symptoms or signs for less than two months and half for less than four, but 1 in 10 had been ill for more than a year The duration of symptoms does not measure the age of the cancer For instance 10 had no symptoms at all although the lesion was large enough to be discovered by radiography; whereas in 5 the first warning of ill health was caused by metastases (hoarseness 3 dysphagia 1 obstruction of the superior vena cava 1) Metastases indicate an advanced stage of the disease, but not necessarily a late one in terms of duration of ill health As expected, the incidence of metastases when the patients were first seen at the hospitals was less in those with shorter histories; nevertheless it was nearly 9% in those with evidence of disease for less than a month It rose to 50% in patients with five months' history On the other hand only 12% of those seen after a year had metastases; presumably this was because of the inherently slow growth and spread of the tumour, or because of the appearance of symptoms at an unusually early stage in its development

History after Coming to Hospital

Treatment

Almost a third (28%) of the patients had clinical or radiographic evidence of metastases when first seen Metastases were found in a further 4% at subsequent examinations and in 9% at bronchoscopy Among the 317 cases thoracotomy was undertaken as follows

- *Exploratory thoracotomy* 81 (25%)
  - Resection 57 (18%)
  - Resection impossible 24 (7%)
- *No thoracotomy* 236 (75%)
  - Metastases 130 (41%)
  - Position of primary 34 (11%)
  - Poor general condition 21 (7%)
  - Poor respiratory function 20 (6%)
  - Refusal 5 (2%)
  - Other reasons 26 (8%)

Thus in 4 out of every 10 cases thoracotomy was not done because intrathoracic or extrathoracic spread was already evident In 11% bronchoscopy showed that the tumour was in such a position that it could not be removed It is difficult to record in categories the other reasons for not operating Frequently there was a combination of factors none of which by itself might have precluded attempting resection In 7% although there was no local evidence of metastases gross wasting indicated that the disease was far advanced. The respiratory function was judged too poor to justify resection in another 6% 5 patients refused investigation or surgical treatment and 3 were incorrectly diagnosed until metastases appeared 1 was not diagnosed until after death

81 (25%) were explored, but the tumour could not be removed in 24 Resection of whole or part of the lung was therefore, carried out in only 57 (18%) of the 317 patients 52 resections were done at the Brompton and 5 elsewhere 12 had radiotherapy in addition—1 before resection 3 shortly afterwards and 8 to metastases that appeared later

120 (37%) were treated by radiotherapy alone (98 at the Royal Marsden Hospital and 22 elsewhere) For analysis the treatment has been called 'palliative' if less than a 4000r tumour dose was given and 'radical'

PHÆOCHROMOCYTOMA AND NEUROFIBROMATOSIS

ADRENOLYTIC EFFECT OF PHENTOLAMINE AND CHLORPROMAZINE

J Knox
M B Glasg , M R C P
ASSISTANT LECTURER

A Slessor
M B Glasg , F R F P S
SENIOR LECTURER

DEPARTMENT OF MATERIA MEDICA AND THERAPEUTICS,
UNIVERSITY OF GLASGOW

Several tests have been developed by which a phæochrome tumour can be diagnosed with certainty before operation. The main problem lies in knowing when to apply these tests, for the clinical manifestations vary considerably. Green (1946) has shown that only 30% of cases have the classic picture of intermittent paroxysms of hypertension first reported by Labbé et al (1922), sustained hypertension is the more common finding.

Smithwick et al (1950) made a notable contribution by drawing attention to certain features commonly associated with hypertension due to phæochromocytoma but uncommon in essential hypertension generalised sweating, vasomotor disturbances in the extremities, unexplained mild fever, increased basal metabolic rate, glycosuria, normal cold pressor test, and postural hypotension and tachycardia.

A further clinical contribution towards suspecting phæochrome tumours was made by Glushien et al (1953), who emphasised the not uncommon association of these tumours with the neurocutaneous syndromes, especially neurofibromatosis. In the following case a phæochromocytoma was suspected because of "dizzy attacks" and mild hypertension in a patient with generalised neurofibromatosis and was found to be present.

Case-report

A kitchen porter, aged 40, was seen in December, 1953, with eight years history of attacks of dizziness and headache. He had been discharged from the Army in 1945 with a medical category A1. Four months later, at a medical examination for re enlistment, he was found to have hypertension. From about that time he began to have sudden attacks of headache lasting a few minutes and preceded by "spots before his eyes". No other symptoms accompanied the headaches which appeared to be spontaneous and came on at irregular intervals. On a previous admission in 1951, he had bilateral apical tuberculosis generalised classical neurofibromatosis, and mild hypertension. After treatment the pulmonary tuberculosis became quiescent, and he remained well until July, 1953, when attacks of headache previously mild and fleeting, became more severe and lasted longer. Each attack consisted in "dizziness" followed by a throbbing frontal headache. When he was seen on Dec 14, 1953, his blood-pressure was 170/120 mm Hg. The association of hypertension and neurofibromatosis suggested that a phæochrome tumour might be responsible for his attacks of headache, and he was admitted for investigation.

On examination he was thin and anxious, with classical neurofibromatosis. Finger clubbing was present. Axillary hair was completely absent but facial and pubic hair were normal. The thyroid gland was normal and the skin dry. No peripheral vasomotor phenomena were observed. pulse was regular, rate 68. No apex impulse was dem strable, sounds of good quality and pure. Blood pressu 160/100 mm Hg. The optic fundi showed early hypertens retinopathy. There were signs of fibrosis at the apex of the lung. No mass was palpable in the abdomen. Nervous system urine, and blood count were normal. Fasting eosinoph 381, 520, and 312 per c mm. Blood urea, plasma-electroly and plasma protein levels, normal. Blood sugar curve insulin sensitivity normal. No paroxysm developed during the latter test. Urinary 17-ketosteroids 15 1 and 10·4 mg 24 hours. Basal metabolic rate (B M.R) +19% and +1 Biopsy of a subcutaneous nodule revealed a neurofibrom

Radiological examination (Dr A Balfour Black and c leagues) —Straight radiography of the abdomen showed small area of calcification above and medial to the upp pole of the the left kidney. An intravenous pyelogram did n show any distortion or displacement of the kidneys. Aort graphy failed because of an electric power fault. Radiograp of the lumbodorsal spine showed kyphosis of the dorsal reg associated with some arthritic changes. No congenit abnormalities.

Special tests for diagnosis —In the *histamine test* a typ paroxysm of hypertension with associated features (fig.) was produced when 0 025 mg of histamine in 0 5 ml of saline solution was injected intravenously. No albumin or sugar appeared in the urine after the test. *Phentolamine test* (Gifford et al 1952) during a phase of mild hypertension (B P 150/100 mm Hg) 5 mg of phentolamine ('Rogitine') given intravenously caused an immediate fall in blood pressure of 30/35 mm Hg. *Combined cold pressor and postural test* (Smithwick et al 1950) change in posture had no effect on the blood pressure or pulse, but immersion of a hand in ice cold water produced a typical paroxysm. *Urinary catechols* (Engel and von Euler 1950) assay of urinary catechols collected on three separate occasio gave 450, 1100, and 1800 μg in 24 hours, expressed adrenaline. The percentage of noradrenaline in the secon and third specimens was 89% and 99% respectively (Dr G West and Mr J J Lewis).

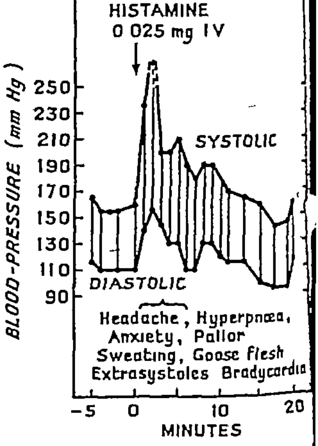

Fig 1—Paroxysm of hypertension duced by intravenous histamine.

Operation (Mr James P Galloway) —Premedication consisted of 'Omnopon' gr $^1/_3$ and hyoscine gr $^1/_{150}$ subcutan ously. In addition 20 mg of intramuscular phentolami was given to prevent the expected rise of blood pressure duri anæsthesia and operation. Anæsthesia (Dr O Watt) w induced with 0 5 g of thiopentone, and immediately thereaft 10 mg of intravenous phentolamine was given. Anæsthes was maintained with nitrous oxide and oxygen, supplemente by two doses each of pethidine (50 mg) and *d* tubocurar chloride (15 mg and 5 mg). Since a plaque of calcificati had been observed radiologically in relation to the upper po of the left kidney, exploration by the left renal approa was undertaken. Applied to the medial side of the upper p of the kidney was a hard mass as large as a walnut, wi vessels running in to the lower pole. The tumour was exc with a small portion of the suprarenal gland spread over superior aspect. Despite the administration of phentolami two hypertensive phases came on during operation (fig When the tumour was excised, the pressure was 90/60 mm. H and an intravenous drip was set up containing 4 mg noradrenaline per pint of saline solution.

Postoperatively on the patient's return to the ward t pressure had fallen to 60 mm Hg systolic owing to a block the drip, but when this was corrected the pressure promptly. The swinging blood pressure in the immedia postoperative period was caused by variation in the speed the infusion. Noradrenaline was continued for 30 hours aft operation, a total of 16 mg being given.

DR BIGNALL REFERENCES

Bignall, J R. Moon A J (1955) In preparation
Boucot, K. R Sokoloff M. J (1954) *Amer Rev Tuberc* 69 164
Brooks W D W Davidson M Price Thomas C, Robson, K, Smithers D W (1951) *Thorax* 6, 1
Bryson C C Spencer H (1951) *Quart J Med* 20, 173
Hill A B (19 2) *Brit med J* ii 1271
Payne, P M (1955) Personal communication.
eneral (19 1) Statistical Review of England and Wales Medical H M Stationery Office
3) *Ibid*
D W (1953) *Brit med J* ii 123

Convalescence was slow because of the reactivation of pulmonary tuberculosis. The attacks of headache ceased and the blood pressure remained steady at 120/80–130/90 mm Hg.

Follow-up.—During the ten months since operation the patient has had occasional attacks of dizziness unaccompanied by headache. After investigation these were attributed to Ménière's syndrome (Dr E. A. M'Connal). The blood pressure has varied between 140/100 and 165/120 mm Hg. Three histamine tests done since operation have been negative. Bio-assay of urinary catechols (Dr G. B. West) has given values of 80, 61, and 115 μg in 24 hours on three occasions. The first and third of these values are above normal, and observation is being continued to determine if another tumour is present.

The tumour measured 4·50 × 3·50 × 2·75 cm., weighed 23 g., and had a dense fibrous capsule. The cut surface revealed solid fleshy brown tissue mottled with grey and red. In the centre was a plaque of calcification. Histologically the tumour had the characteristics of a benign phæochromocytoma (Dr J. Dick and Dr H. Thomson). Bio-assay gave values of 2·644 mg. of noradrenaline and 0·661 mg. of adrenaline per gramme of fresh tissue. The tumour thus contained about 76 mg. of medullary amines, of which 80% was noradrenaline.

Discussion

ASSOCIATION WITH NEUROFIBROMATOSIS

The association of chromaffin tumours with neurofibromatosis was first noted by Eisenberg and Wallerstein (1932), emphasised by Rosenthal and Willis (1936), and reviewed by Glushien et al. (1953), who collected 17 published cases and added 1 of their own. Koonce et al. (1952) have reported 1 other case, and G. Shaw (personal communication) has investigated 1 case.

Although the over-all incidence of neurofibromatosis in published cases of phæochrome tumours is 5%, there seems to be an increasing recognition of the association between these two conditions. Since 1948 11 cases in addition to the present 1 have been reported. Either persistent or paroxysmal hypertension in a patient with neurofibromatosis thus strongly indicates the necessity to search for a phæochrome tumour.

In the present case the diagnosis was amply confirmed before operation. A spontaneous paroxysm was observed in the ward and, although minor in type from the point of view of symptoms, was accompanied by a rise in blood-pressure to 220/140 mm. Hg. Considerable variation in blood-pressure (Labbé et al. 1922, Hamilton et al. 1953) was not observed, but some lability was demonstrable when four-hourly diurnal recordings were made. The intravenous histamine test introduced by Roth and Kvale (1945) was dramatically positive (fig. 1), and more symptoms appeared during the induced paroxysm than in any spontaneous attack. The finding of an excessive amount of catechols in the urine (Engel and von Euler 1950) made the diagnosis certain. But other investigations which are often helpful (Smithwick et al. 1950) were not so in the present case. The glucose tolerance was normal; the B.M.R. was not significantly raised; the fasting eosinophil-count was not low; there was no postural hypotension; and the cold pressor test, often negative in cases of phæochrome tumour, was strongly positive. Compression of the flanks by various means did not produce a paroxysm. Thus, like the clinical picture, the results of the special investigations vary remarkably from case to case.

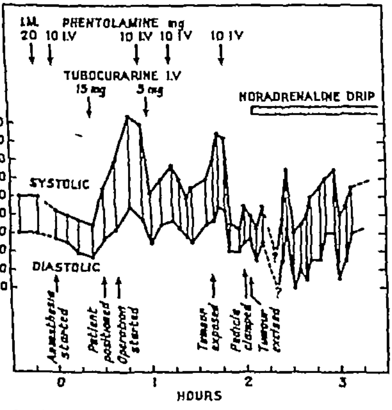

Fig. 1—Changes in blood-pressure during removal of tumour.

Localisation of the tumour, when this is small, is notoriously difficult. The walnut-sized tumour in the present case did not distort the pyelogram, but calcification in the tumour revealed its site. Since Howard and Barker (1937) reported considerable calcification in the tumour of their case, 9 others have been recorded in which flecks or plaques of calcification above one kidney have been of assistance in localisation. Cadman and Tinckler (1953) have reported 2 such cases.

The site of the tumour in the present case was the left suprarenal gland. This is in keeping with the curious observation of Glushien et al. (1953) that when a phæochromocytoma occurs in association with a neurocutaneous syndrome it is usually on the left side. Of the 21 cases reviewed by them the tumour was in the left suprarenal gland in 16 (76%), in the right in 3 (14%), and in both glands in 2 (9%). In reviewing 283 cases of phæochromocytoma without regard to their associated conditions Symington and Goodall (1953) found the left suprarenal gland involved in 33%, the right in 48%, and both glands in 9%. Analysis of these two series of figures indicates that predilection of phæochrome tumours for the left suprarenal gland in cases of neurofibromatosis is not due to chance ($p>0{\cdot}01$ $<0{\cdot}001$). The reason for this is obscure.

PHENTOLAMINE

One of the problems in the management of phæochrome tumours is the acute hypertension which may occur especially during operation. The introduction of adrenolytic agents to control such hypertension has been a major advance. The adrenolytic agent used by us was the imidazoline derivative, phentolamine (C 7337, 'Regitine'), which appears to be more reliable and much less toxic than its predecessor benzodioxane (Emlet et al. 1951, Gifford et al. 1952). The only mention of its use in this country is by Hamilton et al. (1953).

We used phentolamine in the present case for three purposes: (1) to test its adrenolytic effect during a phase of hypertension; (2) to determine if it would prevent the production of acute hypertension by histamine; and (3) to lessen the hazards of aortography and operation.

Effect on Hypertension

Several American workers (Grimson et al. 1949, Emlet et al. 1951, Iseri et al. 1951a and b, Gifford et al. 1952) have shown the hypotensive effect of phentolamine in cases of phæochrome tumour. Emlet et al. (1951) and Gifford et al. (1952) have investigated its value as a diagnostic agent for phæochromocytoma in hypertensive patients, and their results indicate that it is safe and useful. In our patient a phase of spontaneous hypertension was rarely observed; and, when we applied the test by Gifford's technique of 5 mg. intravenously, the blood-pressure fell from 150/100 to 120/65 mm. Hg. This fall of 30/35 mm. Hg is not pathognomonic, for in the series of Gifford et al. (1952) falls of this order were often observed in patients with hypertension due to causes other than phæochromocytoma. Furthermore, these workers emphasise the increased likelihood of false positive results in patients (1) with mild essential hypertension, (2) after sedation or during anæsthesia, and (3) with renal insufficiency

In the preoperative management of patients with adrenaline secreting tumours phentolamine has proved useful in controlling hypertension whether sustained or paroxysmal

Iseri et al (1951a and b) have reported successful use of oral phentolamine in 2 patients awaiting operation

Cahill (1953) and Gifford et al (1952) report the abrupt termination of histamine induced acute hypertension by giving intravenous phentolamine

But in the *prevention* of acute paroxysms of hypertension induced intentionally phentolamine has sometimes failed

In the case reported by Iseri et al (1951b) a paroxysm which would otherwise have been induced by massage of the tumour was prevented by a dose of 25 mg given orally 15 minutes beforehand, whereas on another occasion 2 5 mg given intramuscularly to the patient (a child) was ineffective Bixby and Troncelliti (1952) also record a failure of phentolamine to prevent acute hypertension induced by exercise and by histamine

Effect on Histamine Test

In our patient histamine consistently produced a paroxysm of constant pattern The effect of premedication with phentolamine on the histamine test was to reduce the symptoms substantially while diminishing only slightly the height and duration of the hypertension (compare figs 1 and 3) It is obvious that the doses given (20 mg intramuscularly 20 minutes and 10 mg intramuscularly 4 minutes before histamine) were too small to block completely the large and unknown amount of medullary amines discharged from the tumour The reduction of symptoms is noteworthy Although symptomless hypertension produced by histamine has been reported (Pantridge and Burrows 1951), in our patient all attacks not covered by an adrenolytic agent were characterised by distressing symptoms From the work of Goldenberg et al (1948) and others the symptom-producing amine is adrenaline, noradrenaline causing few symptoms or none It thus seems that phentolamine to a large extent blocks the action of adrenaline and has much less effect on the strongly pressor amine noradrenaline This is in keeping with the findings of Freis et al (1951), who showed that, in a healthy man, phentolamine, though effective in reducing adrenaline induced hypertension, only partially inhibited the pressor action of noradrenaline

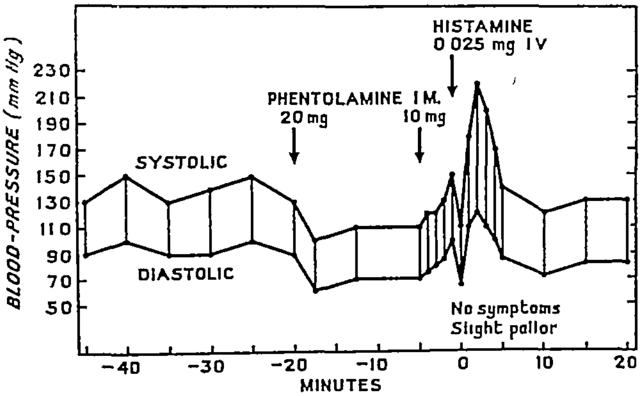

Fig 3—Effect of intramuscular phentolamine on histamine-induced paroxysm of hypertension

Effect on Blood-pressure during Aortography and Operation

st to the partial blocking action of phentolamine [illegible] histamine paroxysm, the blood-pressure [illegible] tely controlled with phentolamine during aortography, which may be fraught with considerab danger in a patient with a phæochrome tumour (Koon et al 1952) This was achieved by giving 20 mg intr muscularly 20 minutes before anæsthesia and 10 m intravenously immediately after induction with 0 5 of thiopentone Anæsthesia was maintained wi nitrous oxide and oxygen During the positioning of t patient and the manipulation of the needle the bloo pressure did not rise above 150/100 mm Hg (fig That he had had a considerable release of sympathe amines during aortography can be inferred from t hypotensive phase which followed the aortography a required noradrenaline for its correction

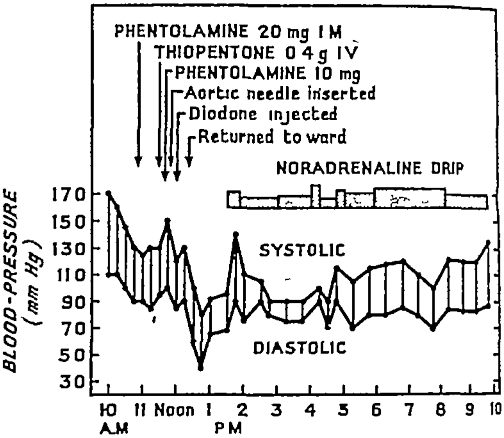

Fig 4—Control of blood pressure during and after aortography

During the operation phentolamine was very effecti in promptly abolishing hypertension when this came (fig 2) It was our object, however, to prevent hyp tension, and in this we were only partly successf Phentolamine 20 mg given intramuscularly 20 minu before anæsthesia, and 10 mg given intravenou immediately after induction, maintained normal blo pressure levels for the first 30 minutes but could prevent a major rise, which began with the injection tubocurarine and continued during the positioning the patient and the early stages of the operation hypertensive phase which appeared imminent after second dose of tubocurarine was aborted by giv intravenous phentolamine 10 mg But this was effective in preventing, 15 minutes later, the rise pressure which followed exposure and handling of tumour

In retrospect it seems that the doses we gave our pati to prevent hypertension were not large enough and not given sufficiently near an expected phase of hyp tension to be effective Yet Cahill (1953) reports that single intravenous dose of 5 mg given early in t operation successfully controlled the blood pressure un the tumour was removed 50 minutes later Emlet et (1951) maintained normal blood pressure for 2 hou after doses of 0 08–0 16 mg per kg (6–12 mg for a m weighing 70 kg), and in the patient of Iseri et al (1951 25 mg orally and 3 mg intramuscularly before operati kept the blood-pressure normal for $2^1/_2$ hours On t other hand, Bixby and Troncelliti (1952) could n prevent a serious rise in blood-pressure during eth anæsthesia by previous injection of phentolamine (do not stated) and by continuous intravenous infusion piperoxane

It is apparent that there is no standard dose phentolamine Although 5–10 mg intravenously w immediately cut short a phase of hypertension, the do required to *prevent* hypertension during operation va from case to case This is not surprising, for the am of sympathetic amine liberated by a tumour will according to the ease with which it can be stimulate by the anæsthetic agents used and by the technical operative difficulties which may arise We had the idea that useful information might be obtained on dosage of phentolamine from our attempts to block the histamine induced paroxysm; but the results though interesting were not helpful Though histamine given intravenously is a potent stimulus of tumour secretion its action is fleeting and poorly reflects the repeated and perhaps prolonged stimulation which can occur during surgical removal.

The special dangers during operation are excessive hypertension acute myocardial failure and postoperative collapse These are due to the large quantities of sympathetic amines released from the tumour especially (1) early in anæsthesia (2) during the positioning of the patient and (3) during the exposure and handling of the tumour To prevent the effects of these amines sufficient adrenolytic agent must already be occupying the receptor sites when they are liberated Since phentolamine seems to be rapidly cleared frequent doses may be necessary

For the prevention of hypertension during operation we suggest (1) administration of 20–30 mg orally or intramuscularly 20 minutes before induction of anæsthesia—Grimson et al (1951) recommend several doses to stabilise the blood pressure before anæsthesia—and (2) 10–20 mg intravenously (*a*) immediately before each of the above mentioned stages of operation when excessive secretion of the medullary amines is expected and (*b*) early on the rising slope of any threatened hypertensive phase Since the amount of amine to be blocked at any time during operation is unknown these doses may have to be modified for the individual case Doses of phentolamine in excess of requirements seem to be harmless because rapid clearance of the drug soon allows normotensive levels to be reached

As regards anæsthetic agents used in operations for removal of secreting medullary tumours certain are contra indicated—e.g cyclopropane chloroform and ethyl chloride (Papper and Cahill 1952) These tend to produce ventricular arrhythmias in the presence of excess circulating adrenaline Ether which is a known stimulant of sympathetic function has been used successfully by Papper but Bixby and Troncelliti (1952) consider it dangerous Thiopentone with nitrous oxide and oxygen were used in the two anæsthesias undergone by our patient For removal of the tumour tubocurarine was also used, and we have the impression that both intravenous doses raised the blood pressure This muscle relaxant is known to liberate histamine (Alam et al 1939) Although in patients without phæochromocytomas the small amount released by rapidly administered intravenous tubocurarine would produce few demonstrable effects, in those having such tumours it might readily release medullary hormones Such patients respond to very small quantities of histamine, in our patient 25 µg consistently provoked a severe paroxysm

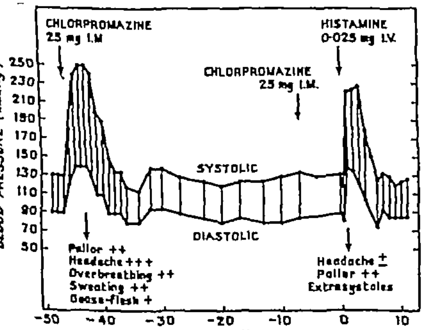

Fig 5—Effect of chlorpromazine on histamine-induced paroxysm of hypertension. The pain of the first injection of chlorpromazine induced a paroxysm (see text).

CHLORPROMAZINE

Courvoisier et al (1953) reported that chlorpromazine possessed adrenolytic properties in the dog the pressor effect of noradrenaline being reduced and the hypertensive effect of adrenaline, given in the same dose as the noradrenaline being abolished In our patient we attempted to find out how effective chlorpromazine would be in abolishing the effects of a mixture of the sympathetic amines liberated from the tumour by histamine Two doses of 25 mg were given 45 minutes and 7 minutes before 0·025 mg of histamine intravenously The first injection of chlorpromazine however, caused the patient some discomfort, and within 30 seconds he developed a typical distressing paroxysm of hypertension (fig 5) The second dose, given with some trepidation gave rise to no untoward symptoms The height and duration of the blood pressure rise provoked by histamine were almost as great as those found in previous tests without blocking agents The symptoms, however were almost abolished (fig 5) Thus like phentolamine chlorpromazine possesses a greater blocking action against adrenaline compared with noradrenaline confirming for man Courvoisier's results in the dog

Summary

A further case of phæochromocytoma associated with neurofibromatosis is reported The provocative histamine test was positive and the diagnosis was confirmed by assay of urinary catechols A plaque of calcification in the tumour localised its site in the left suprarenal gland on radiography

Pre treatment with phentolamine or with chlorpromazine strikingly reduced the symptoms of a histamine-induced paroxysm but influenced the acute-hypertension only slightly

Phentolamine prevented hypertension during aortography but did not prevent two sharp rises of blood-pressure during operation These responded promptly to intravenous phentolamine

The principles governing the use of phentolamine during resection of the tumour are discussed

Tubocurarine given during operation [illegible] phases of hypertension

We are indebted to Dr G B West, [illegible] pharmacology in the University College, [illegible] Lewis, of the department of [illegible] of Glasgow for assays of catechols [illegible] and to Sister Rhoda Grant for [illegible] gations and postoperative [illegible] phentolamine (rogitine) [illegible] courtesy of Mr C W S [illegible]

ISONIAZID IN THE TREATMENT OF PRIMARY PULMONARY TUBERCULOSIS

R McLaren Todd
M A, M.D Camb, M R C P, D C H
SENIOR LECTURER IN CHILD HEALTH, UNIVERSITY OF LIVERPOOL, CONSULTANT PÆDIATRICIAN, ALDER HEY CHILDREN'S HOSPITAL, LIVERPOOL

Isoniazid was first used for treating pulmonary tuberculosis in adults in October, 1951, at the Sea View Hospital, New York (Robitzek et al 1952), and subsequently it has been used for various tuberculous conditions both in adults and in children It has usually been given with streptomycin, but it has sometimes been used alone—e g by Kendig et al (1954), who gave it to patients between 6 months and 5 years old with primary pulmonary tuberculosis They thought that it favourably influenced the course of the disease, but their conclusions were reached after treating only 8 patients and without studying a concurrent series of cases not receiving specific chemotherapy

The present investigation was undertaken to assess more critically the value of isoniazid in primary tuberculosis in children

Plan of Investigation

The children were first seen in the eighteen months between January, 1952, and June, 1953, in the outpatient department of Alder Hey Children's Hospital Many of them had been referred by the chest physicians and tuberculosis officers of the area

50 children were studied, and alternate patients in each of three age groups were given isoniazid, the remainder receiving no specific chemotherapy (table I) The results of tuberculin tests and chest radiography on admission to the investigation, and the history of contacts, are recorded in table II From the history of contact and of such clinical features as erythema nodosum it was possible in most cases to assess the approximate duration of the tuberculosis Table III shows that 43 of the 50 children had had tuberculosis for three months or less on admission to the investigation 4 children were admitted to hospital as inpatients because the adult who was the source of infection had not been removed to sanatorium, but the other children were treated as outpatients

TABLE I—AGE INCIDENCE OF 50 PATIENTS WITH PRIMARY TUBERCULOSIS

Age (yr)	Treated	Controls
Less than 3	8	9
3–6	8	9
7–13	8	8
Total	24	26

The routine therapy for all patients consisted in rest in bed for four to eight weeks, followed by a gradual return to full activity, they also received a diet ade in calories, proteins, and vitamins The treated chil received isoniazid 3 mg per lb body-weight per d divided into three doses a day, for three months. outpatients were seen monthly during the first th months and every three months subsequently At ea attendance they were examined clinically, their and height were recorded, and their chests were rad graphed In view of previous experience of a sim trial with *p* aminosalicylic acid (Todd 1953) white counts and erythrocyte sedimentation rates were estimated.

Results

The patients' progress was assessed in three ways (1) by their vitality and appetite and the re of clinical examination, (2) by records of change body-weight, and (3) by radiological evidence Of 50 children 46 were observed for twelve months, and for nearly three years

TABLE II—DIAGNOSTIC FEATURES IN 50 PATIENTS PRIMARY TUBERCULOSIS

—	Treated		C
Tuberculin test			
Mantoux 1 in 10,000	1		2
" 1 in 1 000	22		15
Jelly	1		9
Radiography			
Focus in right upper lobe	4	15	5
" middle	4		3
lower "	4		8
Right hilar gland	3		5
Focus in left upper lobe	4	9	[illegible]
lower "	2		[illegible]
Left hilar gland	3		1
Known contact	17		21

Clinical examination did not reveal any abnormaliti but the beneficial effect of isoniazid on appetite noticed by the parents in almost every treated case

Body weight on admission was compared with stan weights (Stuart and Stevenson 1950) to ascer whether the treated and the controls were Table IV shows that the initial weights of treated controls were similar The changes in body-weight each of the age and treatment groups were as percentage increases in weight after periods observation of one, two, three, six, nine, and months (table V) The results show no differen in weight gain between the treated and the contr

TABLE III—ESTIMATED AGE OF PRIMARY COMPLEX

Age (mos)	Treated		Controls	
1	9	20	9	23
2	9		9	
3	2		5	
4	2		0	
5	1		1	
Uncertain	1		2	

infants under 3 years of age, but in the two other groups the increase in weight was greater in the tre than in the controls The rate of weight gain in the groups was compared statistically by the t test. In children under 3 years of age and in those over 6 of age there was no significant difference, but in children aged 3–6 years there was a significant differen those receiving isoniazid gained weight more rapidly th the controls

Radiographs taken after three, six, and twelve mo were compared with those taken at the first visit and results recorded in table VI Increase in the X ray sha is indicated by +1, +2, or +3, an unchanged sh by 0, and decrease in the shadow by −1, −2, or −3 (c plete resolution) There may be difficulty in interpr the significance of the radiological shadows seen

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DR KNOX, DR SLESSOR REFERENCES—*continued*

Grimson K S, Emlet J R, Hamblen E C (1951) *Ann Surg* 134, 451
— Longino F H Kernodle C E O'Rear H B (1949) *J Amer med Ass* 140 1273
Hamilton M Litchfield J W Peart W S, Sowry, G S C (1953) *Brit Heart J* 15 241
Howard J E, Barker W H (1937) *Bull Johns Hopk Hosp* 61 371
Isérl L T Chandler D Myers G B, Boyle A J (1951a) *J Mich med Soc.* 50 1370
— Henderson H W Derr, J W (1951b) *Amer Heart J* 42 129
Koonce D H Pollock B E, Glassy, F J (1952) *Ibid* 44 901
Labbé M Tinel J, Doumer (1922) *Bull Soc med hôp Paris* 46 982
Pantridge J F, Burrows M M (1951) *Brit med J* 1 448
Papper E M, Cahill G F (1952) *J Amer med Ass* 148 174
Rosenthal D B Willis R A (1936) *J Path. Bact* 42 599
R[illegible] M. Kvale W F (1945) *Amer J med Sci* 210, 653
[illegible] R. H Greer W E R., Robertson C W, Wilkins, (1950) *New Engl J Med* 242, 252
[illegible] T Goodall A L (1953) *Glasg med J* 34, 75

TABLE IV—COMPARISON OF BODY WEIGHTS ON ADMISSION

Age (yr)	Percentile distribution	Treated	Controls
ess than 3	25th percentile	2	2
	50th	4	5
	75th	2	2
–6	25th	8	7
	50th		1
	75th		1
–13	25th	6	5
	50th	1	2
	75th	1	1
Total		24	26

primary tuberculosis. In some cases a definite diagnosis of segmental collapse can be made, and confirmed by bronchoscopy, as in 2 of our patients, but in other cases it is impossible to distinguish consolidation from collapse. In most of our cases we took the view that the radiological shadow was due to enlarged mediastinal glands with an adjacent primary focus. After three months the shadow tended to clear earlier in the treated patients. 14 of the 24 patients showed radiological improvement compared with only 8 of the 26 controls. Statistical analysis however does not show that this difference is significant. After six months and after twelve months there were no differences between the treated and the controls.

The period which elapsed between the onset of the primary complex and the radiographic appearance of calcification in the hilar glands or at the site of the primary focus was also compared in the treated and the controls. This assessment was made after the patients had been observed for at least seventeen months, and some for thirty months, and it was found that calcification was present in 14 of 20 treated patients and in 17 of 20 controls. The average interval between primary complex and calcification in both groups was seventeen months (maximum twenty-eight, minimum ten months).

TABLE V—PERCENTAGE WEIGHT GAIN ABOVE INITIAL WEIGHT

Age (yr)	At 1 month	At 2 mos.	At 3 mos	At 6 mos	At 9 mos	At 12 mos
Less than 3						
Treated	1·1	3·4	6·3	10·1	16·7	23·0
Controls	0·0	5·2	7·7	14·4	18·2	25·7
–6						
Treated	2·5	3·0	6·5	6·0	13·7	22·3
Controls	0·0	0·4	2·7	5·2	6·1	10·1
–13						
Treated	3·1	4·7	7·1	10·5	12·5	16·1
Controls	1·0	5·0	4·4	7·2	10·1	12·2

Complications encountered were few. 2 treated patients aged 6 years and 7 years showed radiological evidence of rupture of a caseous gland into a bronchus about six months after their first visit as outpatients. The diagnosis was confirmed by bronchoscopy, the caseous material was removed, and both patients made an uninterrupted recovery.

One of the controls, aged 10 weeks when first seen, the youngest patient observed in this investigation, developed tuberculosis of the left hip eighteen months after his first visit, although the primary pulmonary lesion had healed by calcification.

There were no deaths.

Discussion

The beneficial results of chemotherapy with streptomycin, *p*-aminosalicylic acid, and isoniazid and the introduction of other measures are reflected in the decrease of the crude death rates from all forms of tuberculosis from 552 per million people in 1947 to 202 per million in 1953. Many of the patients who have survived did so in spite of the fact that they had the more serious tuberculous conditions, such as miliary tuberculosis, tuberculous meningitis, and advanced pulmonary tuberculosis.

It might be thought that specific treatment at the earliest stage of tuberculosis (primary complex) would be more effective than after the development of complications, but this has not been the general experience of pædiatricians and others who have given either streptomycin or *p*-aminosalicylic acid to children with primary tuberculosis.

Lorber (1950) found no beneficial effect of streptomycin in children with a primary tuberculous complex.

Todd (1953) found no benefit from *p*-aminosalicylic acid in 35 children with primary pulmonary tuberculosis compared with 34 controls. In a further small controlled series of 12 children under the age of 3 years, with uncomplicated primary pulmonary tuberculosis, combined therapy with streptomycin and *p*-aminosalicylic acid did not have any demonstrable effect (Todd, unpublished).

TABLE VI—RADIOLOGICAL CHANGES

Degree of change	After 3 mos		After 6 mos.		After 12 mos	
	Treated	Controls	Treated	Controls	Treated	Controls
+3	0	1	0	0	0	0
+2	2	0	2	1	0	0
+1	1	4	2	2	0	0
0	7	12	1	7	2	2
–1	12	9	7	14	1	4
–2	2	0	9	2	14	18
–3	0	0	0	0	3	2
Total	24	26	21	26	20	26

The prognosis of primary tuberculosis in children varies with their age and with the age of the primary complex (Wallgren 1946). In children over the age of 3 years serious complications are uncommon, but if they do arise this usually happens within three months of the development of the primary tuberculous complex. These facts should be taken into account in any assessment of the possible beneficial effects of specific drug therapy. In the present series 43 of the 50 children were first seen within three months of the development of the primary lesion. Isoniazid seemed to have a beneficial effect on the patients' general health, judged by improved appetite and by the gain in weight observed in the children aged 3–6 years and those aged more than 6 years, although in the latter the gain in weight was not statistically significant. There also appeared to be improvement in the radiographic appearances of the treated patients when compared with the controls three months after the start of treatment, but this difference also was not statistically significant. Although the ultimate prognosis, judged on clinical grounds and on the appearance of calcification, was similar in the two groups, we formed the impression that isoniazid therapy was more often associated with decrease in size of the primary lesion during the first three months of the illness, and this is at a time when the danger of developing serious complications is greatest. A larger series of patients will have to be studied to find out if this impression is correct.

The possible harmful effects of isoniazid should also be considered. Side-effects such as vertigo, headache, drowsiness, twitching of the lower limbs, hyperreflexia, dryness of the mouth, agranulocytosis, and sulphæmoglobinæmia have been reported, but they were not observed in this series. Bacterial resistance to isoniazid is a serious complication that develops during treatment of adults with phthisis. The Medical Research Council (1953) found resistance in 9% of 181 positive cultures after a month's treatment, in 40% of 147 positive cultures after two months' treatment, and in 81% of 132 positive cultures after three months' treatment with isoniazid. Similar results have been obtained in other investigations, in which either streptomycin alone or *p*-aminosalicylic acid alone was given to adults with phthisis.

This has not been our general experience with chemotherapy of tuberculous children, but we have observed streptomycin resistance in 3 of 55 patients with tuberculous meningitis (Capon and Todd 1949) and in 1 of 8 patients with tuberculous bronchopneumonia (Todd 1949) Sweetnam and Murphy (1954) discussed the possible emergence of resistant strains of tubercle bacilli in children with miliary tuberculosis treated with isoniazid alone They considered that, because of the relatively small amount of fibrous tissue reaction, there was no barrier to the action of isoniazid, and that the development of drug resistance was therefore only a very remote possibility In the present investigation no attempt was made to isolate tubercle bacilli from gastric washings and to estimate the sensitivity to isoniazid, because the patients were living at home, but, from the satisfactory progress they made, it is unlikely that they suffered harmful effects from this form of chemotherapy

Summary

Isoniazid, 3 mg per lb body weight per day, was given to alternate patients, in a series of 50 children with primary pulmonary tuberculosis, for three months

The children receiving isoniazid gave a better clinical response than did the controls, particularly as regards appetite The gain in body-weight of children aged 3–6 years was significantly greater in the treated than in the controls X-ray shadows also tended to clear earlier in the treated than in the controls The clinical and radiological condition after from one to three years did not differ in the treated and the controls

The risk of the development of drug resistance is discussed

A larger series of patients will have to be studied to find out whether isoniazid is of value in the treatment of primary pulmonary tuberculosis

I wish to thank Prof Norman B Capon for his help and advice, and Mr R L Plackett, M.A, of the department of applied mathematics in the University of Liverpool, for help with the statistics

REFERENCES

Capon, N B, Todd, R M (1949) *Practitioner*, 162 414
Kendig, E L jun, Trevathan, G E Ownby, R. jun. (1954) *Amer J Dis Child* 88, 148
Lorber, J (1950) *Lancet*, i 389
Medical Research Council (1953) *Ibid*, ii, 217
Robitzek E H, Selikoff, I. J, Ornstein, G G (1952) *Quart Bull Sea View Hosp* 13, 27
Stuart, H C Stevenson S S (1950) *In* Textbook of Pediatrics Edited by W E Nelson Philadelphia
Sweetnam W P, Murphy E F (1954) *Arch Dis Childh* 29, 338
Todd R M (1949) *Brit med J* i 741
— (1953) *Ibid*, i, 1247
Wallgren A (1945) *Amer J Dis Child* 70, 263

COMBINED LEFT PNEUMONECTOMY, THORACOPLASTY, AND LIGATION OF PATENT DUCTUS ARTERIOSUS

J R Edge
M D Leeds, M R C P
CONSULTANT CHEST PHYSICIAN

J S Glennie
M D Aberd, F R C S E
CONSULTANT THORACIC SURGEON

HIGH CARLEY HOSPITAL, ULVERSTON, LANCASHIRE

Successful ligation of a patent ductus arteriosus was first described by Gross and Hubbard in 1939, and since then this operation has become a commonplace of cardiac surgical practice If the condition is left untreated the ex[illegible]n of life is much reduced, owing to the risk of [illegible]larteritis and of endocarditis, and of cardiac [illegible] the increased work done by the heart as a

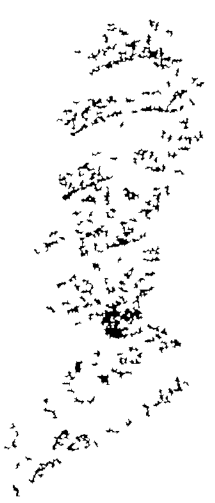

Fig 1—Radiograph of chest, Aug 3, 1954

result of the shunt The operative mortality is as as 2–3% (Gross 1947, Crafoord 1948), but Wood (19 advises against operating routinely on mild symp free cases

Surgical resection of lung tissue for tuberculosis been practised from time to time since the first report Tuffier in 1891, but both the immediate mortality and the subsequent morbidity from bronch pleural fistula remained extremely high until the adv of chemotherapy

Conklin et al (1951) reported favourably on practice of combining thoracoplasty and resection in single operation, they used this technique when presence of disease in the opposite lung, or in any ing lung on the operated side, made it advisable to over expansion of the residual lung tissue, with attendant risk of reactivation In this hospital combination of resection and thoracoplasty in operation has been standard practice in suitable cases the past year

We have been unable to find any reported instance of patient undergoing pneumonectomy, thoracoplasty, ligation of a patent ductus arteriosus at a single opera as in the case described here

Case-report

A housewife, aged 35, with four children was found to be early pulmonary tuberculosis in 1943, when radiography her chest showed limited infiltration in both upper zones. this time she was told that there was "a murmur in heart" After a short period of general treatment in sanatorium she was kept under observation as an o and she remained quite well until 1952, when she became with severe anæmia and persistent slight pyrexia admission to hospital at that time she had typical signs patent ductus arteriosus, and the spleen was palpable, cultures on three occasions showed a heavy growth of α hæmolytic streptococci The infective endarteritis was treated penicillin 250,000 units three hourly and streptomycin 0·5 twice daily, for six weeks, her symptoms were comple relieved, the fever settled, and subsequent blood cultures negative She was then referred to another hospital, ligation of the ductus was considered but not proceeded wi Radiography of her chest at this time showed no evidence reactivation of tuberculous disease, and she returned to household duties She remained well until early 1954,

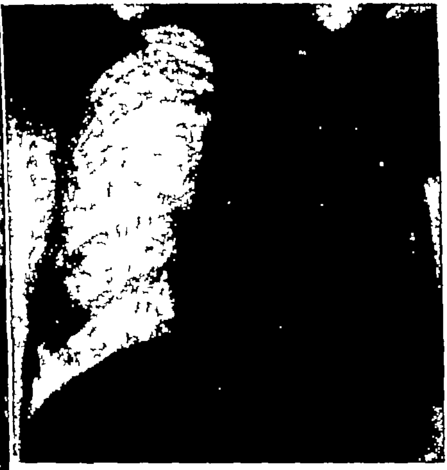

Fig 2—Radiograph of chest fifteen days after operation.

she developed a productive cough felt very unwell and lost weight She was first seen by one of us in May 1954

On examination her general condition was poor There was a continuous murmur together with a systolic thrill, in the second left intercostal space the blood pressure was 100/30 mm. Hg There was no finger-clubbing Radiography showed considerable spread of the tuberculous disease in the left upper lobe where there was a large homogeneous oval opacity—evidently a blocked cavity—and there were scattered though limited fresh opacities in the right upper zone The heart was not greatly enlarged, but screening in the left anterior oblique position revealed some prominence of the left ventricle The sputum was positive for tubercle bacilli for the first time

On admission to High Carley Hospital on Aug 2 her general condition had greatly deteriorated she was feverish and extremely ill, and radiographic examination (fig 1) showed that the contents of the lesion in the left upper zone had been evacuated leaving a large thick walled cavity; there was extensive bronchogenic spread of disease to the left lower zone mainly to the lingula

Treatment with postural rest and chemotherapy (streptomycin 1 g. daily and isoniazid 250 mg daily) was begun and after two months there was very striking improvement in her general condition. Radiography showed blocking of the large cavity in the left upper lobe some slight contraction of the massive spread in the left lower zone and almost complete disappearance of the small lesions in the right lung Bronchoscopy revealed no sign of significant endobronchitis; blood cultures were repeatedly negative

At this stage—no doubt because of her considerable symptomatic improvement and numerous domestic anxieties—the patient became very restless and it seemed unlikely that she would accept long-continued hospital treatment We had therefore to consider immediate definitive treatment for her condition was clearly still precarious The risk of circulatory failure following pneumonectomy in the presence of a patent ductus with increased pulse pressure was unquestionably grave We therefore decided to do a thoracotomy to ligate the ductus, and (if the patient's condition was still satisfactory) to proceed there and then to resect the diseased lung tissue We calculated that the risk of bronchogenic dissemination of disease following thoracotomy would be considerable unless the tuberculous lesions could be dealt with at the same time

Operation (Nov 1)—The dissection of the ductus was complicated by the presence of many adherent glands the vessel the wall of which was not unduly thickened was ligated with two floss silk ligatures The radiographic finding of disease limited largely to the upper lobe was confirmed by palpation; dissection of the hilum was extremely difficult owing to the presence of many glands adhering to the pulmonary artery and its main branches and in freeing one of these glands the main pulmonary artery was damaged and could not be repaired It was consequently necessary to proceed to pneumonectomy instead of to lobectomy as intended On completion of the pneumonectomy the patient's general condition remained satisfactory and so the upper four ribs were removed to minimise the likelihood of subsequent mediastinal displacement

Progress—The postoperative course was singularly uneventful; within a few days the patient's general condition had greatly improved and all signs of toxæmia had disappeared the blood pressure became established at 120/60 mm Hg and the continuous murmur was replaced by a short low pitched mid systolic pulmonary bruit The radiographic appearance fifteen days after operation is shown in fig 2

At the time of publication the patient remains in excellent health, has no cough or sputum, and does not complain of dyspnœa on ordinary exertion She is up all day and will be discharged home in the next few weeks.

Summary

A woman aged 35 with extensive pulmonary tuberculosis and patent ductus arteriosus previously complicated by infective endarteritis was successfully treated by combined ligation of the ductus, pneumonectomy and thoracoplasty at a single operation

Our thanks are due to Dr C P Brown, whose skill in anæsthesia made this operation possible and to Dr A. P B Waind for information about the patient when she was under his care in 1952 for the treatment of infective endarteritis.

REFERENCES

Conklin, W S Tuby J E. Grismer J T (1951) *J thorac Surg* 22 271

Crafoord C. (1948) *Brit Heart J* 10 71

Gross, R E. (1947) *J thorac Surg* 16 314

— Hubbard J P (1939) *J Amer med. Ass* 112 729

Tuffier M. (1891) *Bull Soc anat. Paris* 66 300

Wood P (1950) Diseases of the Heart and Circulation London; p 228

NEW SHORT-ACTING THIOBARBITURATE

PETER NOBES
M.B Lond. F.F.A. R.C.S D.A
ANÆSTHETIC REGISTRAR, CHASE FARM HOSPITAL AND THE ENFIELD GROUP OF HOSPITALS MIDDLESEX

IN anæsthesia for outpatients both hexobarbitone and sodium thiopentone have the great disadvantage that somnolence may persist after the operation

Weese and Koss (1954) and Dietman (1954) have described experimental and clinical experience with 'Baytenal' a new very short acting anæsthetic which is apparently eliminated from the body so rapidly that its administration is followed by little, if any postoperative somnolence

This drug is sodium 5 5 allyl (2 methyl propyl) thiobarbiturate. It is issued as a powder, which is readily soluble in water and is administered as a 10% solution which according to the manufacturers is stable for thirty six hours It is not at present on sale in this country

Weese and Koss (1954) based their observations on 350 cases

Their series included inpatients many of whom were ill and debilitated these were given premedication but morphine and its derivatives were avoided Outpatients were given no premedication and all types of surgical oper[illegible] lasting up to 10 minutes were undertaken. [illegible] the av[illegible] adult they injected 2–3 ml. of the 10% s[illegible] rapi[illegible] and after about 1½ minutes a further

TABLE I—FINDINGS WITH BAYTENAL IN FIVE INPATIENTS

Case no	Age (yr.)	Sex	Operation	Premedication	Dose of baytenal (g.)	Duration of unconsciousness (min.)	Time after initial injection until patient sat unaided (min.)	Nausea or vomit
1	28	F	Removal products of incomplete abortion	Omnopon gr. $^1/_3$, scopolamine gr. $^1/_{150}$	0·5	$16^1/_2$	30	Momentary retch on recovery
2	54	F	Sigmoidoscopy and biopsy rectal neoplasm	Omnopon gr. $^1/_3$, scopolamine gr. $^1/_{150}$	0·5	14	40	Slight retching awakening
3	36	M	Perianal injection 'Proctocaine'	Omnopon gr. $^1/_3$, scopolamine gr. $^1/_{150}$	0·45	6	16	Nil
4	25	M	Incision ischiorectal abscess	Nil	1·0	7	11	Nil
5	[illegible]	M	Manipulation of left knee	Omnopon gr. $^1/_3$, scopolamine gr. $^1/_{150}$	0·6	4	27	Nil

on the depth of narcosis or duration of operation. In no case did the total dose exceed 1 g. Where muscular relaxation was needed succinylcholine was administered.

Weise and Koss emphasise that, because of the freedom from subsequent excitement, the slight respiratory depression, and, above all, the very rapid elimination of this drug, the patients needed no supervision after *operation: there was no vomiting or other complication. Outpatients were able to leave the operating-theatre within a few minutes of the end of the operation, and to go home in 20–30 minutes.*

Clinical Trial

A clinical trial of baytenal has been undertaken at Chase Farm Hospital. Because little of the drug was available the series included only eleven patients. Their ages ranged from 17 to 62, and, in order to obtain an unobscured picture of the effects of the baytenal, cases were selected to exclude so far as possible those where the addition of long acting relaxants, inhalational agents, or other intravenous drugs would be necessary.

The inpatients, with one exception, received premedication with 'Omnopon' gr. $^1/_3$ and scopolamine gr. $^1/_{150}$. The outpatients received no premedication, with the exception of one who was given atropine gr. $^1/_{100}$. Baytenal was given mostly in a single dose, injected as rapidly as possible. The dose was estimated on the basis of the patient's age, weight, and general condition and the probable duration of the operation. During anæsthesia some patients breathed air, while others received a nitrous oxide/oxygen mixture at the rate of 5 and 2 litres per minute respectively either immediately following the injection or after several minutes where return of consciousness seemed likely before the end of the operation. Particular attention was directed to the duration of unconsciousness, judged by the time taken by the patients to register complete awareness of surroundings in response to questioning. The degree of respiratory depression, the time which elapsed before the patients were able to sit or walk unaided, and the presence or absence of excitement, amnesia, and nausea or vomiting were noted.

The results are summarised in tables I and II.

Experimental Observation

The drug was administered experimentally to a volunteer (P. N.).

The blood pressure was recorded and spirometry trac were taken by two observers. No premedication was gi the spirometer facepiece was applied, and time given become accustomed to the apparatus.

Baytenal 0·6 g. was given slowly over a period of minutes. Rapid loss of consciousness occurred, preceded b brief sensation of drowsiness; no taste was experienced blood pressure fell from 138/90 to 120/80 mm. Hg and pulse rate rose from 72 per minute to 120 per minute. slight depression of respiratory amplitude was registered on spirometer, but respiratory rate was unchanged. Afte further $1^1/_2$ minutes baytenal 0·4 g. was injected as qui as possible. This injection was followed by a slight fall in rate and volume of respiration, which returned to nor within 2 minutes. 2 minutes after this second injectio painful stimulus (digital pressure over the brachial ple caused increased depth and rate of respiration.

6 minutes after the initial injection the subject rega consciousness. He had no mental confusion whatever was able to answer questions regarding time and pl there was no retrograde amnesia. After a further 6 min he was able to walk in a straight line, and within 22 min from the first injection was able to write an account of jective sensations. The return to full consciousness was re Slight euphoria persisted for about 2 hours, but this n way impaired the sense of wakefulness, nor the ability drive a car and carry on with normal work within that per This contrasted strongly with the 3–4 hours of pronoun somnolence experienced by the subject after 0·2 g. of sod thiopentone a week previously.

Discussion

The most striking feature in this series was the short time in which patients regained normal consci ness with freedom from postanæsthetic confusion drowsiness. Equally important was the very s interval between recovery of consciousness and re of ability to sit, stand, and walk unaided. Du anæsthesia respiratory depression was very slight, in no case (except where succinylcholine was used) apnœa of more than a few seconds' duration app Retching occurred in only three cases, and lasted about $^1/_2$–1 minute; two of these three patients received omnopon gr. $^1/_3$ and scopolamine gr. $^1/_{150}$ premedication. In five cases a normal meal was tal within 2 hours after the anæsthetic. It would seem th if the "single dose" technique is used, at least 0·5 should be given to an adult patient.

Baytenal may prove of special value for casualty outpatient cases where it is particularly desired to av

TABLE II—FINDINGS WITH BAYTENAL IN SIX OUTPATIENTS

Case no	Age (yr.)	Sex	Operation	Premedication	Dose of baytenal (g.)	Duration of unconsciousness (min.)	Time after initial injection until patient sat unaided (min.)	Nausea or vomiti
6	61	F	Reduction of Colles fracture	Nil	0·4	5	10	Nil
7	61	M	Incision septic thumb	Atropine gr. $^1/_{100}$	0·75	$9^1/_2$	13	Nil
8	25	F	Incision breast abscess	Nil	1·0	15	28	Sl. moment. retch
9	55	F	Manipulation of knee	Nil	0·25	1	Immediate	Nil
10	[illegible]	F	Manipulation of ankle	Nil	0·5	$2^1/_2$	$3^1/_2$	Nil
11		M	Manipulation of knee	Nil	0·45	4	7	Nil

the unpleasantness of induction with an inhalation anæsthetic but where it is also important that the patient is ambulant within a very short time Because of its rapid elimination it may be worth trying its administration by continuous drip infusion for longer operations. The contra indications to sodium thiopentone should be applied equally to baytenal though this drug causes less severe respiratory depression and may thus be more suitable for " poor risk " cases.

Summary

A new short-acting thiobarbiturate ' Baytenal ' has been tested in eleven patients and in a healthy volunteer

This drug depresses respiration very slightly

It may prove particularly useful for anæsthesia in outpatients because of the rapid return of consciousness and the absence of postanæsthetic somnolence and confusion

My thanks are due to Dr P W S Gray and Dr D Zuck, consultant anæsthetists to Chase Farm Hospital, for their help and encouragement in the preparation of this paper I am also grateful to Messrs Bayer of Leverkusen Germany for a supply of Baytenal

REFERENCES

Dietman, K. (1954) *Chirurg* 25, 155

Weese H., Koss, F H (1954) *Dtsch med Wschr* 79 601

Medical Societies

ROYAL SOCIETY OF MEDICINE

Induced Hypothermia

THE anæsthetics section met on April 1 under the chairmanship of Dr BERNARD JOHNSON president of the section to discuss Induced Hypothermia

Dr C. F SCURR observed that tissue anoxia due to circulatory arrest unless rapidly relieved led to cellular death ; but if the body temperature was lowered cellular metabolism and oxygen demands were reduced so the cells survived the anoxia for longer periods A hypothermic technique might be valuable for intracardiac operations for transposition of the great vessels for operations for congenital cyanotic heart-disease, for certain intracranial operations, and for some abdominal and thoracic operations such as excision of an aortic aneurysm. There were five advantages to be gained First, the oxygen requirements of the tissues were reduced since if shivering was prevented oxygen consumption fell in a linear fashion with fall of body temperature Secondly cardiac work was reduced Thirdly the coagulation *time of the blood was increased which* might be beneficial in certain types of cardiovascular surgery where thrombosis was a potential danger Fourthly anæsthetic requirements were reduced Fifthly harmful bacterial and enzyme activity was suspended Dr Scurr noted several disadvantages which necessitated special care on the part of the anæsthetist such as a tendency towards carbon-dioxide retention a shift to the left in the oxyhæmoglobin dissociation curve and a retardation in the elimination of non volatile anæsthetic agents Moreover the heart rate cardiac output and blood pressure were all decreased with a tendency to cardiac irregularities at levels around 25°C Such irregularities presaged ventricular fibrillation ; and because of this continuous electrocardiographic control was in Dr Scurr's opinion essential Sinus bradycardia with normal complexes had usually been seen in his cases. During rewarming after cooling might occur owing to the opening up of the peripheral circulation with the transfer of very cold blood to the main circulation A further fall in the central temperature from this cause might lead to ventricular fibrillation and death

Dr SCURR described how he induced hypothermia in small children under light anæsthesia and oxygen perhaps with a muscle relaxant to prevent shivering He used a cooling blanket through which circulated water at 2–4°C

Dr T C GRAY (*Liverpool*) described the results of induced hypothermia in 110 patients almost all adults He advocated surface cooling and demonstrated the technique with a colour film Hypothermia was induced during light anæsthesia with a muscle relaxant, and under the vasodilator effect of chlorpromazine There was no shivering and an adequate temperature fall could be obtained in one and a half hours The tendency towards an ' after drop ' in temperature when active cooling ceased could be prevented by tilting the patient at fifteen minute intervals to prevent local accumulation of blood. Dr Gray showed that this ' after-drop " was most common in patients with a large surface area whose temperature fell slowly during cooling He thought that this technique was altogether more satisfactory than intravenous administration of a mixture of chlorpromazine, promethazine hydrochloride, and pethidine followed by surface-cooling which was slow in effect and often complicated by shivering

He and his colleagues had used induced hypothermia for intrathoracic neurosurgical, and general surgical operations Hypothermia had also been produced therapeutically, but without *conspicuous success.* In neurosurgery its particular value seemed to be the increased safety with which induced hypotension could be used for long periods with the patient in the upright position, while in general surgery a low temperature seemed to *offer some protection against the effects of surgical* trauma this was most obvious in poor risk patients. In the whole series of 110 cases there were 13 deaths These were very *poor risk patients* but 3 of the deaths among patients submitted to neurosurgical operations were *from pulmonary embolus and Dr Gray thought* there might be some significance in this

Attempts to measure the pituitary adrenal responses of patients to surgical stress with and without induced hypothermia had not yet shown much difference, but *from experimental work on dogs Dr Gray thought* there was evidence that these responses were modified to the ultimate benefit of the animal

In the discussion that followed, Dr J W DUNDEE (*Liverpool*) remarked on the particular value of induced *hypothermia for neurosurgical cases* In one case he described the surgeon had clamped the middle cerebral artery for seven and a half minutes without postoperative sequelæ.

Dr B G B LUCAS remarked on the difference between *the tolerance of the brain and of the heart for ischæmia* during induced hypothermia The heart was more susceptible under these conditions than the brain—a reversal of the order at normal temperature—which suggested that the future of very deep hypothermia might lie in methods of *reducing heart work*

Mr C E DREW suggested that hypothermia was of great value for operations on congenitally cyanotic children particularly when it was not possible to tell preoperatively what surgical procedure might be necessary The antithrombotic effect was probably of value when an anastomosis was performed

Dr G J REES (*Liverpool*) doubted whether hypothermia was ever of value for the Blalock shunt operation He remembered anæsthetising a child with congenital heart-disease and cyanotic coma—*a very severe case*—with a successful outcome He considered that if this was possible with a standard *anæsthetic technique* then it was unnecessary to submit the child to further risks

Reviews of Books

Brain Mechanisms and Consciousness

A Symposium organised by the Council for International Organisations of Medical Sciences Consulting Editors EDGAR D ADRIAN, United Kingdom, FREDERIC BREMER, Belgium, HERBERT H JASPER, Canada Editor for the Council J F DELAFRESNAYE Oxford Blackwell Scientific Publications 1954 Pp 556 42*s*

THE members of this symposium met to discuss eighteen papers which they had already circulated among themselves These papers, with condensed verbatim reports of the ensuing discussions, form the substance of this book

The matter falls into three categories First, experimentalists describe the rousing effect of thalamic stimulation on the massed electrical activity of the cerebral cortex in various animals, and trace impulse traffic in cortex and reticular formation with micro electrodes Second, clinicians show that consciousness in man is disturbed by molesting centrencephalic tissue, and investigate the psychical correlates of abnormal electro encephalograms which parallel those artificially induced in animal brains Third come some broader based psychobiological essays which come really closest to the purpose of the symposium

Nerve impulses reach the cerebral cortex from the receptors along topographically organised channels An unsolved problem, as Lord Adrian points out, is the nature and site of the blocking process that has to be invoked to explain how, of all signals thus reaching the cortex, some are attended to and some are not The main afferent pathways are distinguished, in contemporary theory, from "non-specific" reticulo-cortical projections which diffusely activate the cortex Our scientific heirs may not agree with the notion that these so-called non specific projections constitute a single system, and may smile on the mid-twentieth-century tendency to view the reticular formation as a single anatomical and functional entity

Full publication of such proceedings is necessary for the specialist, but makes for an unwieldy book The report might have been more acceptable if it had taken the form of a précis devised by a single writer, but truncation of the massively intelligent essays of Fessard, Hebb, and Láshley would be unforgivable. This account leaves a strong impression that the study of consciousness is still a proper province for psychological and philosophical investigators, and that the neural complexity already revealed by the physiologists can provide as many neural models as may be required, without enforcing the claims of any one of them

Diagnostic cytologique du cancer génital chez la femme

RAYMOND BOURG, professeur a l'Université Libre de Bruxelles, CLAUDE GOMPEL, assistant a l Institut Jules Bordet, Centre des Tumeurs de l'Université Libre de Bruxelles, JEAN PAUL PUNDEL, agrégé de l'Enseignement Supérieur Liége Desoer Paris Masson 1954 Pp 348 Fr 4800

Clinical Cytology

Using the May Grünwald Giemsa Stained Smear Vols I and II P LOPES CARDOZO, M D, consulting physician and lecturer in hæmatology and cytology, Universities of Leyden and Amsterdam Leyden L Stafleu 1954 Pp 128 and 191 72 50 guilders

INTEREST in cytological methods of tumour diagnosis is spreading on the Continent Partly because Papanicolaou's work which was the first to gain wide recognition for cytological methods, was in this field, and partly perhaps because it is more susceptible to mass-production methods than any other, vaginal cytology has nearly always occupied a prominent place in studies on cytological tumour diagnosis, and the first of these two books is concerned solely with this technique The views expressed, backed by an experience of 15,000 examina- unspectacular but sound The illustrations usual lithograph-like quality which in these days of ever-glossier reproduction is grateful to the e and seems to involve no loss of detail

Dr Cardozo's book is more unusual He hold hæmatology to be the first branch of diagnostic cytolog and claims the whole subject as a legitimate exten of the methods of hæmatology His use of hæmatolog techniques in staining cells is characteristic

He deals with skeletal lesions—using especially a "preci location" puncture of localised lesions, often under th fluoroscope—cervical lymphadenopathies, thyroid tum lung tumours, both by sputum and by direct puncture c pleural and ascitic fluids A chapter on diagnosis of prost carcinoma, using cytological examination of material expres by prostatic massage, is contributed by Dr J Posthuma n claim for 96% of positive smears in prostatic cancer pr justified this may prove a most valuable new method.

Dr Cardozo is an enthusiast, and sometimes a litt less than fair to other methods of diagnosis, but he written a readable book, valuable especially for unconventional approach to a subject often treated rather narrow lines The translation is just imp enough to retain a flavour of the original language witho losing anything in sense, and the coloured phot micrographs (in a separate volume) are excell Only the price is likely to detract from a deserv popularity

Dental and Oral X-Ray Diagnosis

A. C W HUTCHINSON, D.D S, M.D S, F D S, F professor of dental surgery, University of E Edinburgh and London E & S Livingstone 19 Pp 524 75*s*

THE 29 chapters of this book range from develop and normal anatomy through dental pathology to ger diseases of bone Professor Hutchinson is not a r logist, and this has its disadvantages and perhaps advantages

The reproduction of the intra oral radiographs among many illustrations of wide range is good Unfortunately extra oral views are rarely of the same standard, for most them are too dark X ray films are notoriously difficult reproduce, as many authors sadly discover, but it is a pity the high standard of reproduction of the dental films has been maintained in those of the skull and jaw All obl lateral radiographs of the mandible and temporomandib joint have been printed as if viewed from the tube side— is, through the patient—while intra orals (quite are presented as viewed outside the mouth Thus the teeth in the two groups appear to belong to opposite and this is confusing The anatomy is well presented, pathology is extensively and, in most instances, well Description of the radiographic appearances is more me There is a full bibliography after each chapter

Apart from some minor errors this is a valuable notably for its collection of radiographs P Hutchinson offers his readers sound advice, based on experience, on the value and limitations of radiograp evidence

Nerve Blocks

A Manual of Regional Anesthesia for Practitioners Medicine JOHN ADRIANI, M.D, director, department anesthesiology, Charity Hospital of Louisiana Springf Ill Charles C Thomas Oxford Blackwell Sc Publications 1954 Pp 265 47*s* 6*d*

Dr Adriani is well known and respected as a of several lucid and factual works on anæsthetic sub and this volume on local analgesia is an admi addition to his series It is not complete, nor is it int to be, but it does give a very clear and helpful acco of the principal techniques, including those of spinal epidural analgesia Although in this country gen anæsthesia is usually preferred to any form of local, th procedures still have many valuable uses, not only surgery but in therapeutics

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Connective Tissues—The Josiah Macy, jun., Found New York, has published the transactions of the conference this subject held in February, 1954 The editor is Dr Ragan. (1954 Pp 222 $4 25)

THE LANCET

LONDON SATURDAY APRIL 16, 1955

Scoliosis

CURVATURE of the spine may manifest itself at most any time during the period of growth, and articularly in early adolescence There are many nown causes, but the ætiology of the ordinary or "idiopathic," scoliosis is quite unknown. The ancients ave little to say on the subject, and even ANDRY who coined the word "orthopædics ") is for once at loss Later workers have tended to accept the views well expressed by ROYAL WHITMAN[1] Lateral urvature was regarded as one of the penalties of the rect posture The predisposing conditions were eneral weakness from any cause fatigue from over ork, and all factors that might enhance the difficulty f holding the trunk erect under the pressure of the uperincumbent weight Both heredity and occupa on were thought to be exciting factors , and even abitual posture—for example, slouching at a school esk of the wrong height and the posture during eep—was incriminated Later, psychological factors ere taken into account BLUNDELL BANKART used tell his students "you recognise the presence of scoliosis by looking at a child's back, but if you ant to find the cause you look at the mother's face nd the boring teacher rather than ill designed school urniture was blamed for slouching

This approach has led nowhere It is only during e past few years that serious attempts have been ade to solve the problem NACHLAS and BORDEN[2] oduced curvature in dogs by preventing growth on ne side of the vertebral bodies where the epiphyses ere bridged with staples SOMERVILLE[3] on the basis experimental evidence described a chain of events ading to scoliosis which was initiated by structural rdosis arising from failure of growth of the posterior ements of a segment of the spine (i e, all those arts of the vertebræ lying behind the bodies) ARKAS[4] after a detailed anatomical pathological nd radiographic study has advanced a somewhat ifferent view He describes different processes for e thoracic and lumbar regions Thoracic curves start o believes, in the cervicothoracic segment during e first four years of life and several years may pass efore the middle and lower thoracic regions are volved He believes that the basic pathological rocess consists in separation of the epiphyseal ring om the rest of the vertebral body and its partial splacement Moreover he thinks that this separation preceded by an infantile form of osteoporosis of e spine Lumbar scoliosis he attributes to con nital anomalies in the articular system of this region hich permit rotation of the vertebræ Perhaps the ews of both SOMERVILLE and of FARKAS will prove to be soundly based, because it is most unlikely that all "idiopathic" scolioses have a single cause, but much has yet to be learnt before either view can be accepted

The treatment of structural scoliosis is singularly difficult because the bones of the vertebræ are abnormal in shape Ideally the deformity would be prevented from occurring at all, but this is hardly feasible until more is known of the ætiology Deformity in the adult cannot be corrected, the shape of the fully grown bone can be changed only by carpentry, which so far has proved impracticable Attention has therefore been directed chiefly to preventing increase in deformity after this has been recognised, and to influencing the forces acting on the developing bones in such a way as to modify their shape during growth It can hardly be said that scoliosis was treated at all, until a generation ago when the great pioneers of orthopædic surgery attacked the disorder with corrective plaster casts spinal braces and gymnastics They succeeded, by close attention to detail by dogged perseverance, and above all by displaying such enthusiasm as secured the willing coöperation of the patient, in giving many a potential victim the semblance of an erect posture But no cure was possible no scoliotic could be made straight, and the most that could result from years of conscientious work by surgeon, physiotherapist, and patient was a balanced and reasonably supple body Today little more than this is possible, and modern methods are no more than refinements of the old The plaster cast applied during extension has been replaced by the hinged cast associated with the name of RISSER, the brace has been greatly improved, notably by BLOUNT, of Milwaukee and any correction gained can now be held by fusing long lengths of the spine. A few brave surgeons have strayed from the well trod paths The latest of these are ALLAN,[5] of Birmingham, who has inserted into the spine an apparatus with an internal turnbuckle which spans the concavity of the curve and forces the ends apart, and ROAF[6] of Liverpool, who in specially selected cases has excised a wedge from the vertebral bodies at the apex of the curve Such operations are still on trial

It is difficult to compare the results of the later methods with those of the earlier, because only in the past few years has it been possible to assess the prognosis in an individual patient In the past many underwent years of energetic treatment including spinal fusion, even though the curve was of a type unlikely to progress, and the results were correspondingly favourable Now thanks to the work of PONSETI and FRIEDMAN,[7] JAMES,[8] and several others, it is possible to foretell at an early stage and with reasonable accuracy, which curves are likely to develop to a crippling degree Modern reports of the results of treatment refer only to the curves likely to become severe—about 5% of all—for these are the only ones that are now subjected to energetic treatment whereas the older surgeons included scoliosis of every pattern and grade The best that can be achieved with a very severe curve is to reduce the angle by perhaps 50% and restore, or greatly improve, the balance of

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Whitman R. A Treatise on Orthopædic Surgery Philadelphia 1927

Nachlas, I W, Borden, J N *Surg Gynec Obstet* 1950 92 672 See *Lancet* 1951 ii, 434

Somerville E. W *J Bone Jt Surg* 1952 34B 421

Farkas A *Ibid* 1954 36A, 617

[5] Allan F G *Ibid* 1955 37B, 92.

[6] Roaf R *Ibid*, p 97

[7] Ponseti I V, Friedman B *Ibid* 1950 32A, 38

[8] James J I P *Ibid* 1954 36B, 36

the trunk The patient (more often a girl) thus reverts to a condition in which, when fully clothed, she is not obviously deformed and can face the world with greater equanimity The price she pays for this is a long stay in hospital, with immobilisation in a grotesque position and perhaps several major operations, and her back may still become painful later in life

What of the lesser thoracic curves that are treated only by remedial exercises designed to keep the body supple and of the lumbar curves that often pass unrecognised for many years ? These are not so unsightly as to be an embarrassment during youth, but only too often they give rise to crippling pain in later life They are very much commoner, and they present an even greater challenge to the surgeon, than the more severe deformities Here there has been no real advance in a thousand years we can neither prevent them from starting nor influence their course We are unlikely to do so until as much effort is directed to ætiology as is now devoted to the mechanics of treatment

Infection Before Birth

INTRA-UTERINE infection as a cause of perinatal mortality has not attracted the attention it deserves Forty years ago SLEMONS[1] indicated that placental bacteræmia was an important cause of fœtal death late in labour, and BROWNE[2] subsequently drew attention to the occurrence of intra-uterine pneumonia Yet relatively few detailed pathological and bacteriological studies of this condition have been described DOUGLAS and STANDER[3] showed that blood-cultures from infants stillborn after prolonged labour associated with intrapartum infection were usually positive, and in over half of this group the placenta showed histological evidence of acute infection LABATE[4] demonstrated pathological evidence of pneumonia in 8% of 868 consecutive necropsies of stillborn or neonatal infants CORNER and his associates[5] stated that asphyxia was the most important pathological finding in 79% of 53 stillbirths and neonatal deaths associated with prolonged labour Of their whole series of 1233 perinatal deaths 82 (6 6%) were found at necropsy to be due to infection, the commonest cause was pneumonia, which was often associated with prolonged labour and evidence of " chorioamniotitis " SIDDALL[6] demonstrated inflammatory changes in the placenta, amnion, chorion, and umbilical cord

It seems that many newborn who develop pneumonia in the first week of life have been infected in utero AHVENAINEN[7] found a surprisingly high incidence (63%) of pneumonia in 674 necropsies of live born infants in the Children's Clinic, University of Helsinki , in 15% pneumonia was judged to be the sole cause of death Half of these children died in the first week of life, but surprisingly there was no convincing statistical evidence that the incidence of pneumonia was higher after complicated than after uncomplicated labours , nor was there a close correlation with neonatal asphyxia BLANC[8] sised the importance of early diagnosis of infecti the newborn The time interval, anoxia, micro virulence, and prematurity may all influence relationship between maternal and fœtal infecti symptoms of maternal infection and the co of labour are not reliable guides to the of the fœtus In his opinion ascending infec never involves the fœtus in the absence amniotic inflammation He detects such inflam tion by placing on a slide a shred of am from near the large placental vessels with its plac surface downwards, and staining this as with a sm Examination of endotracheal or gastric fluid aspir from the infant gives immediate proof of contamina

Other workers, seeking to combat infection prom have made out a case for the prophylactic tration of antibiotics to the mother when labou prolonged, particularly when the membranes been ruptured for some hours CHARLES[9] has cribed interesting work on the placental transm of antibiotics WOLTZ and his associates[10 11] rep in 1945 that penicillin crossed the placental b as early as the tenth week of pregnancy , and peni given late in labour was detected in the fœtal bl concentrations of from a quarter to a half that i maternal blood[12 13] Clinical experience, notab the treatment of syphilis,[14] supported these la findings , and subsequently the passage of str mycin, chloramphenicol, and aureomycin throug placenta was reported Ross et al[15 16] point the need for maintaining a high maternal blood of antibiotic to ensure transference to the f CHARLES now concludes that penicillin, strepton chloramphenicol, aureomycin, and tetracycline a transferred from the maternal to the fœtal orga in therapeutic concentrations Of these subst all except penicillin enter the liquor amnii or negligible amounts Penicillin is retained in the amnii, where its level remains high even afte maternal serum level has greatly fallen T difficult to explain since all these substances similar molecular weight and apparently the sodium, and possibly other constituents of the am fluid are rapidly exchanged with the mat serum[17 18] CHARLES suggests that the am membrane absorbs penicillin selectively

EASTMAN[19] states that in the managemen uterine inertia " because of the threat of intrapa infection whenever the membranes rupture pr turely it is customary to administer penicillin sulphadiazine in cases in which the membranes been ruptured 12 hours or more " In this co such a practice is perhaps less usual , for the emerg resistant strains of staphylococci has tempered husiasm for large-scale prophylactic administration antibiotics Bowie[20] points to the increasing portance of staphylococci in genital tract infections is highly desirable that we should know what tential pathogens exist in the genital tract fore embarking on the administration of anti tics and when labour is prolonged the practice, lowed by Charles, of plating high vaginal abs within twenty four hours of rupture of the mbranes seems sensible It is generally agreed at administration of antibiotics is not indicated in e "latent interval" between spontaneous rupture the membranes and the onset of labour Eastman[21] marks that in his series intensive antibiotic therapy roughout this latent period neither prevented trapartum infection nor affected perinatal mortality

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[1] Slemons J M *J Amer med Ass* 1915 65 1265
[2] Browne F J *Brit med J* 1922 ii, 590
[3] Douglas R G Stander H J *Amer J Obstet Gynec* 1943, 46 1
[4] J S *Ibid* 1947, 54 188
[5] W Kistner R. W Wall R L *Ibid* 1951, 62 1086
[6] S *Ibid* 1950 60 1281
[7] E K *Ann Med intern Fenniæ* 1953, 42 1
[8] Blanc W A *Gynæcologia* 1953 136 101
[9] Charles, D *J Obstet Gynæc Brit Emp* 1954, 61 75
[10] Woltz, J H E Wiley, M. M *Proc Soc Exp Biol* 1945 60 105
[11] Woltz J H E Zintzel H A *Amer J Obstet Gynec* 50 338
[12] Green H J Hobby G L *Proc Soc exp Biol, N Y* 57 282
[13] Herrell W E Nichols D R Heilman F R *J Amer Ass* 1944 125, 1003
[14] See *Lancet* 1954 ii 1268
[15] Ross S Bischoff, H , Preisser W , Orr, W *J clin* 1949 28, 1050
[16] Ross S Burke F G Sites J Rice, E C , Washington *J Amer med Ass* 1950 142 1361
[17] Flexner L B Cowie D B Hellman L M Wilde W Vosburgh, G R *Amer J Obstet Gynec* 1948 55, 469
[18] Vosburgh G J Flexner, L B Cowie D B Hellman L Proctor N K Wilde W S *Ibid* 1948 56 1156
[19] Eastman N J *Obstet Surg , Bull* 1955, 10, 16, Wil Obstetrics New York, 1950, p 780

Systemic Lupus Erythematosus

The diagnosis of systemic lupus erythematosus as become so fashionable that physicians can be rgiven for thinking that it is a newly distinguished ndition But this is not so sixty years ago ir William Osler[22] described almost all aspects f the varied clinical picture that we now recognise arvey et al.[23] have lately reviewed this disorder at ngth and have described 138 cases seen at Johns opkins Hospital, Baltimore

In systemic lupus erythematosus skin lesions may s Osler recognised) be absent, or they may consist f the well known "butterfly" erythema on the face r a discoid lesion, and the course varies from acute and hort to chronic and lasting many years Harvey and is colleagues agree with Arnold[24] and Haserick[25] ho use the term "systemic lupus erythematosus" r the generalised form of the disease, and the terms discoid" and disseminate" only for the skin sions They suggest that the clinical picture varies much that it is useless to classify the disorder into stinct types Like others they found that most of eir patients (78%) were females 80% were aged 5-40 years In no less than 55 out of 105 cases that ere carefully analysed allergic manifestations, such s urticaria or hay fever or sensitivity to various rugs, were recorded but in only 20 of these cases did uch manifestations appear before systemic lupus was iagnosed. Harvey et al list twenty four diagnoses ade by various physicians in the early stages, hey fall roughly into the groups pyrexia of unknown rigin," rheumatic diseases blood diseases skin iseases, diseases of the central nervous system and functional illness In the 105 cases that were nalysed the initial manifestations were related most ommonly to joints 34 were diagnosed as acute igratory polyarthritis' and 16 had arthralgia ever was the leading sign in 24 patients and some ort of erythematous skin lesion in 21 fatigue and eakness were the main complaints in 18, weight ss in 7, other initial symptoms were much less ommon As might be expected in the course of the sease most patients showed weight loss skin lesions, and joint disorders, and 65 had some abnormality of the urine What is more surprising is that 78 patients had a hæmoglobin level below 11 g per 100 ml and 26 had thrombocytopenia, 56 patients had pleurisy, 16 with effusion, as many as 45 had pericarditis Enlargement of lymph glands was detected in 58 patients, this was generalised in 34 Splenomegaly was found in only 15, but the liver was enlarged in 32 Analysis of skin lesions showed that a "butterfly" rash had been present in 39, mucosal lesions in 14, and a purpuric rash in 9 In 27 patients a "typical rheumatoid arthritis with deformity' was recorded The thrombocytopenia of systemic lupus erythematosus may be indistinguishable from the "idiopathic' form, and a full increase in platelets may follow splenectomy, nor does the microscopic appearance of the spleen given any guidance The platelet-count remains high until the patient ultimately dies from the other effects of systemic lupus In the Johns Hopkins series a useful clue in 6 cases, was that discoid lesions preceded the purpura, but in others there was no preliminary sign. It is no wonder that Harvey and his colleagues say that "the disease may appear with a confusing array of manifestations resulting from multisystem involvement in which it is difficult to detect any obvious continuity Joint and, with somewhat lesser frequency, mucocutaneous manifestations are commonly present in episodic fashion and are helpful in pointing towards the correct diagnosis"

With so complex a clinical picture, it is not surprising that physicians turn to the laboratory for help in diagnosis The "L.E cell phenomenon," originally described by Hargraves and his co workers in 1948 is the basis of the most useful test for confirming the diagnosis[26] The phenomenon is now known to be due to a plasma factor associated with the gamma globulin fraction. With proper technique it can be detected using only the patient's own blood, no bone marrow or normal polymorphs are needed Harvey et al use heparinised blood from the patient and examine the buffy coat. They think that other techniques, especially those using clotted blood, are more liable to give false-positive results They obtained positive results in 82 out of 96 patients known to have systemic lupus erythematosus whose blood was examined and in a group of over 700 patients with clinically similar skin, joint, blood, and other symptoms due to various other diseases, there were no positives at all Another laboratory test that has been helpful is examination of the plasma proteins Of the 105 Johns Hopkins patients 58% had serum globulin levels of over 3 g per 100 ml., and values in excess of 4 g per 100 ml. were not unusual In half the patients albumin amounted to less than 3 5 g per 100 ml, and in some it was lower than 2 g per 100 ml. The plasma fibrinogen level was found to be increased in every case where it was tested Electrophoresis also showed high fibrinogen and high gamma globulin levels Other plasma protein tests have given results that are too variable to be useful Biopsy of lymph nodes skin, and muscle, though it has been widely practised seldom yields a pathognomonic picture Thus in Harvey's group of patients lymph node biopsy was inconclusive in 11 and positive

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0 Bowie H *Edinb. med J* 1954 61 Transactions of the Edinburgh Obstetrical Society p 1

1 Eastman N J *Obstet Surv Baltimore* 1955 10 16

2 Osler W *Amer J med Sci* 1895 110 629

3 Harvey A. McG, Shulman L. E. Tumulty, P A Conley C L., Schoenrich E. H *Medicine Baltimore* 1954 33 291

4 Arnold H Jun *Arch. Derm Syph* 1950 62 63

5 Haserick J R *J invest Derm* 1951 16, 211

[26] See *Lancet* 1951 ii, 110

in only 2, of 19 skin biopsies 12 were positive, and out of 12 muscle biopsies only 1 was positive

No fewer than 34 of the patients who had *not* been treated with hormones had remissions lasting at least a year, in most of these patients the remissions lasted one to four years, but some were free of signs of active disease for ten years or more 12 patients had more than one remission in the course of their illness Commonly the remissions affected only some aspects *of the disease, and complete relief with return to full* activity over a period of years was unusual Administration of corticotrophin or cortisone is now the treatment of choice 62 of **Harvey**'s patients were treated in this way After this treatment was discontinued the disease remained quiescent or mildly active in 26%, in a further 18% quiescence persisted with maintenance treatment, in *the disease continued to progress* 18 patients (2 died, 9 of them during treatment **Harvey** and co workers point out that corticotrophin and corti are not specific remedies, and they agree with and **Bader**[27] that the best that can be expected that some patients will be maintained in remission some time The difficulty in treating systemic lu with cortisone or corticotrophin is that car vascular complications often develop, this happ in about half of the patients treated, but Har et al point out that these complications can controlled and do not regard them as a indication to continued administration

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27 Soffer L J Bader R *J Amer med Ass* 1952 149

Annotations

TRAINING THE NURSE

In nursing experiments are in the air—some of them, perhaps, too much in the air Several of those suggested by the Scottish Standing Nursing and Midwifery Committee,[1] however, seem well worth trying After the publication, in 1953, of the Nuffield job analysis of the work of nurses in hospital wards,[2] the standing committee appointed subcommittees to examine that report in detail and make recommendations This report is based on their findings Among other things the standing committee suggest an experiment in two year training, and another in a three year comprehensive training The two-year course, they say, might be tried for five years to assess its value The student nurses should, if possible, live in a building, separate from the hospital, where they should receive their theoretical teaching and develop their corporate life—a sort of college, in fact From this they would go out to appropriate hospitals in the neighbourhood, for their ward training The students would be carefully selected, of good secondary school standard in education, and not younger than $18^1/_2$ The annual intake would not be more than 30, and the teaching staff would include not fewer than 3 sister tutors and 2 " clinical instructors "—a new grade of teacher, having the status of ward-sister but with some training in teaching, who would give them their ward instruction We have always believed that a two year training course would be possible for nurses, provided they were given proper student status—as in this experiment they would be The committee foresee that the curriculum might cover a wide range of subjects, including medical, surgical, gynæcological, psychiatric, pædiatric, ophthalmic, dermatological, and obstetric nursing, communicable diseases (including tuberculosis), operating theatre and ear-nose and throat work, experience of outpatient work, and domiciliary visiting The whole course would be designed to link the theory and practice of nursing in a logical manner—an experiment which we should dearly like to see tried

The committee have also considered the possibility of a three-year course, to be conducted in a hospital or group of hospitals already training nurses The student nurses would gain experience in general nursing and also, for *short periods, in special fields including mental disorder*, infectious diseases and tuberculosis, sick children, and public health The committee say that student nurses on this course would need "to be given student status to a greater degree than is given to student nurses now" but they clearly do not contemplate giving them the full student status suggested for those taking the two-year course The chief advantage of this plan to be that it would bring the student into touch aspects of nursing which at present she may encounter in general training It is disappointing, ever, that the committee have not included, these, geriatric nursing or the care of the chronic

Another important recommendation is that the method should be tried—the patients in each ward divided into groups of about a dozen, and each being assigned to the care of a small team of nurs team would normally consist of a staff nurse, a training, and a nursing auxiliary, and these them would attend to all the needs of the patients care Such group assignment of patients has ofte advocated, and some experiments have already made by now reports on them should be available system has many advantages—the chief one bein the nurse comes to think in terms of " patients," of " rounds " of this or *that type* of duty It also weaknesses, one being that off-duty times and interruptions oblige all the nurses in the ward after all the patients some of the time, instead of the nurses looking after some of the patients all time The committee have sought to overcom difficulty by providing a relief team to take ove group of patients in turn, so that all the membe team are off duty together, but they admit that t for a fairly lavish supply of nurses They reco that special funds should be found for an expe on these lines

Their proposal for the creation of a new grade—"clinical instructor" already mentioned—perhaps d rather cautious consideration They argue that sisters have not much spare time, and that most o have had no training in teaching They therefore that a nurse who has spent two or three years as nurse and has taken a course—of about six wee teaching should be able to instruct students in wards in nursing techniques Two people may ably object to this suggestion the ward siste might not welcome the entry of another woman o status into her domain, even though her righ responsibilities (as the committee insist) wou amply protected, and the sister-tutor, who i qualified to give clinical instruction but seldom a to put her nose inside the wards A more w appointment would surely be that of a coordina studies, whose main task might well be to reconcile sisters to the thought of a ward round conducted sister-tutor In any case, clinical teaching should be given by a senior person—whether ward sister or tutor—rather than by a nurse still considering w or not to take a higher qualification What the sister needs is time, and what the sister-tutor ne access surely these could be provided without the duction of a new grade of teacher who might affront

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1. The Work of Nurses in Hospital Wards H.M Stationery 1955 Pp 19 9d

The Nuffield Provincial Hospitals Trust, 1953 See 1953 1 379

I N N

IT is no easy task to find suitable "official" names for new drugs. The W.H.O. Expert Committee on the International Pharmacopœia, which aims at obtaining international coöperation in the selection of such names, proposes[1] that the initial letters I.N.N. (international non-proprietary name) should be inserted after the name of the drug where this is internationally approved. The committee suggests that the naming authority of the country in which a drug originates should bear in mind the principles on which an international name is selected: this should ensure that such a name will prove internationally acceptable. The name should be short, it should avoid confusion with other drugs, and it should give some indication of the principal chemical groupings, but be free from any therapeutic suggestion. Various syllables are recommended to indicate certain pharmacological groups. These include the suffixes "-ine" for alkaloids and organic bases, "-in" for glycerides and neutral principles, "-caine" for local anæsthetics, and "-stigmine" for anticholinesterases.

National naming authorities have already shown their willingness to coöperate by submitting some 300 proposed names to the expert committee. If only international collaboration of this order had been achieved half a century ago!

ELECTROCARDIOGRAPHY AS A SCREENING TEST

A SINGLE comprehensive test for detecting heart-disease would be highly valuable, and it is hardly surprising that in the U.S.A. electrocardiography (E.C.G.) has been used for this purpose. At present its limitations seem to outweigh its advantages. Despite some evidence that lead I by itself is hardly inferior, multiple leads are generally regarded as necessary, and these cannot conveniently be recorded in a mass survey. Moreover, the criteria of normality are in doubt. Minor signs such as extrasystoles, uncomplicated axis-deviation, slurring of QRS, and T wave changes in lead III, can be ignored; but borderline prolongation of P-R, QRS, and Q-T, and flattening of the T wave in left-ventricular leads, will often make interpretation difficult. Generous standards are obviously necessary to allow for normal variations and for changes due to age, posture, and body build. The effects of a recent meal may be important, especially since, as Levitt and Dinman[2] have shown, they can reverse pathological inversion of the T wave. Even when those factors have been taken into account, it is still not easy to assess the worth of the E.C.G. as a screening test. Graybiel et al.[3] found it useful in excluding disease in young airmen; and Philips[4] thought it the best single test for heart-disease, with a success-rate of 65% in case finding among 2250 people. Dawber and his colleagues[5] found 50–60% of cases in 2000 subjects, with little difference whether lead I alone or the twelve conventional leads were used; they also found 18% of false positive records.

Sprague[6] has proposed an electrocardiographic grading for the assessment of job fitness in railwaymen; but Durham and McGee,[7] after sixteen years' experience including the examination of 3700 electrocardiograms from 7400 industrial workers, find the electrocardiogram unhelpful in prognosis. It would be a pity if this or any other single test were allowed to justify hard and fast rules for the employment of patients with heart-disease. The prognosis of heart disease—particularly of infarction and degenerative myocardial conditions—is now known to be much better than was formerly thought, and a patient's capacity for work of any kind can be judged only by his performance. There is even evidence that exercise within limits may improve the prognosis. As Durham and McGee point out, it is the duty of those who examine workers with heart-disease to educate employers to a greater understanding of their potentialities.

PREVENTING RHEUMATIC FEVER

THE risk of recurrent rheumatic fever in a patient who has had one attack is considerable; nine years ago Hansen[1] estimated it as 60–75% in the three years after an initial bout. This risk is associated with respiratory infection (possibly mild or unnoticed) with group A streptococci, whose rôle in the pathogenesis of the disease is now undisputed. By prophylaxis this risk can be greatly reduced. Stollerman[2] has compared the effect of prophylaxis with sulphadiazine, oral penicillin, and repository benzathine penicillin. Despite its apparent disadvantages (risk of serious toxic effects and occasional bacterial resistance) sulphadiazine comes out of the comparison very well. In nearly three thousand "patient seasons" studied by many investigators the sulphonamide prophylaxis groups showed a recurrence rate 85% lower than that of the control groups. With oral penicillin results are good and serious toxicity is rare; but the minimum effective dose is not clearly established, and at the recommended level (200 000–250 000 units daily or twice daily) the cost of continuous prophylaxis is not negligible. Intermittent prophylaxis with larger doses (800 000 units daily for the first week in each month) has given favourable results,[3] but the cost would be no less. Both oral penicillin and sulphadiazine have the disadvantage that breaks are likely in the daily routine of taking the tablets. As an alternative the new repository penicillin compound benzathine penicillin, administered intramuscularly once a month in doses of 1 200 000 units, has so far given very good results; but the pain at the injection site is considerable, and it is not yet certain whether reactions are commoner with benzathine penicillin than with penicillin by mouth. Neither oral[4] nor benzathine[5] penicillin in the usual dosages significantly increase the penicillin resistance of pharyngeal strains of viridans streptococci; but with benzathine penicillin the blood level of the drug, though sustained, is very low, and does not afford protection against, for example, bacterial endocarditis.

Discussing group A streptococcal respiratory infections Stollerman rightly remarks on the importance of prompt and adequate treatment with penicillin. There is now much solid evidence that if the course of penicillin suffices to eradicate streptococci from the throat, the risk of a subsequent initial attack of acute rheumatic fever is greatly reduced.[6] Early treatment continued for seven to ten days both eradicates the streptococcus from the pharynx and suppresses antibody response to the organism as measured, for example, by the antistreptolysin test.[7] These two effects have been to some extent separated and studied in an investigation by Catanzaro et al.[8] In this American trial involving nearly 1200 cases of group A streptococcal pharyngitis in young adults a group of patients received delayed penicillin treatment, starting on the ninth day after the onset of symptoms. Control groups either received no treatment or were treated with sulphadiazine from admission The antistreptolysin response to the streptococcal infection was about the same in all the groups, but in the penicillin group the incidence of subsequent rheumatic fever was much lower than in the untreated and sulphadiazine-treated groups

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[1] World Health Organization. Expert Committee on the International Pharmacopœia: Sixth Report of the Subcommittee on Non-proprietary Names. WHO/Pharm/280 Oct. 19, 1954.

[2] Levitt, B. M., Dinman, B. D. *J. Amer. med. Ass.* 1955, 157, 122.

[3] Graybiel, A., McFarland, R. A., Gates, D. C., Webster, F. A. *Amer. Heart J.* 1944, 27, 524.

[4] Phillips, L., Chapman, J. M., Goerke, L. S. *Ibid*, 1953, 45, 319.

[5] Dawber, T. R., Kannel, W. B., Love, D. E., Streeper, R. B. *Circulation*, 1952, 5, 559.

[6] Sprague, H. B. *Industr. Med.* 1948, 17, 279.

[7] Durham, R. J., McGee, L. C. *Arch. intern. Med.* 1951, 41, 918.

[1] Hansen, A. E. *J. Pediat.* 1946, 28, 296.

[2] Stollerman, G. H. *Amer. J. Med.* 1954, 17, 757.

[3] Kohn, K. H., Milzer, A., MacLean, H. *J. Amer. med. Ass.* 1953, 151, 347.

[4] Krumwiede, E. *Pediatrics*, 1949, 4, 634.

[5] Stollerman, G. H., Rusoff, J. H. *J. Amer. med. Ass.* 1952, 150, 1571.

[6] See *Lancet*, 1953, i, 278, 285; *Ibid*, March 19, 1955, p. 603.

[7] Wannamaker, L. W., Rammelkamp, C. H., Denny, F. W., Brink, W. R., Houser, H. B., Hahn, E. O., Dingle, J. H. *Amer. J. Med.* 1951, 10, 673.

[8] Catanzaro, F. J., Stetson, C. A., Morris, A. J., Chamovitz, R., Rammelkamp, C. H., Stolzer, B. L., Perry, W. D. *Ibid*, 1954, 17, 749.

If the antistreptolysin response indicates the response to other streptococcal antigens it may be concluded, as Cantazaro et al point out, "that the prevention of rheumatic fever by penicillin treatment of streptococcal disease is not related to the suppression of the immune response ordinarily seen" On the other hand, the results suggest that the living streptococcus must be present for rheumatic fever to develop although this organism has rarely been detected in the joints, blood, nodules, or heart valves of rheumatic patients These workers suggest, too, that their results make the "auto antibody" hypothesis regarding the ætiology of rheumatic fever less tenable, but knowledge of the biological mechanisms of antigenicity and tissue antibody response is at present so fragmentary that it is difficult to substantiate either this argument or the alternative hypothesis of hyper sensitivity to "streptococcal products" Nevertheless, analysis of the effects of antibiotic treatment of strepto coccal infections may yield further information on the pathogenesis of rheumatic fever

ATYPICAL TUBERCULOSIS OF THE LIVER

In patients with tuberculosis the liver may be affected in many ways, either directly as a result of the spread of infection to the liver or indirectly as a result of the metabolic disturbance Amyloid degeneration and severe fatty infiltration are the two outstanding types of hepatic disease due to such metabolic disturbance But, apart from these severe changes, impaired liver function can commonly be revealed in tuberculous patients by function tests Involvement of the liver owing to bacterial dissemination is also by no means uncommon, especially in the late stages of tuberculosis when the incidence may rise to 80% Jaundice is rare, there was only a single case in Cruice's [1] series of 570 necropsies on patients who had died of chronic pulmonary tuberculosis, and only 7 in his 1748 clinical cases of tuberculosis Tuberculosis of the liver is therefore easily overlooked in the diagnosis of chronic jaundice, especially because the clinical picture closely resembles that of infective hepatitis Since the prognosis of hepatic tuberculosis has been vastly improved by antibiotics and chemotherapy the recognition of such cases is important

Cleve et al [2] have now described 4 cases under the title "atypical tuberculosis of the liver with jaundice" This is defined as a condition "where the liver is principally or exclusively involved in tuberculous infection and where there are signs and/or symptoms of hepatic involvement" All 4 patients were Filipino men of military age The commonest clinical features were mild to moderate persistent obstructive jaundice, low-grade pyrexia often accompanied by chills, hepatomegaly, and upper abdominal pain unrelated to meals Liver-function tests suggested parenchymal hepatic injury, there was increased thymol turbidity and bromsulphalein retention In only 1 case was there evidence of active pulmonary tuberculosis, in 2 others there was radiographic evidence of quiescent pulmonary disease It is not surprising that the correct diagnosis was made only with the aid of laparotomy, even then in the 1st case the raised white hepatic nodules were mistaken for metastatic neoplasms until histological examination revealed the characteristic changes and acid-fast bacilli Laparotomy is apparently the only certain method of confirming the diagnosis, which cannot be reliably excluded by a negative Mantoux reaction or by repeatedly needle-biopsies

Treatment with streptomycin 1 g daily has prod some dramatic results Of the 4 patients treated in t way by Cleve et al 2 apparently recovered comple seven and twelve months after the end of treatm An equally satisfactory result has been reported i other cases [3 4] Atypical tuberculosis of the liver jaundice is undoubtedly a rare condition in this c where the resistance of the viscera, excluding the l is high In other communities visceral suscepti may be much greater, and Cleve's series of 4 cas Filipinos suggests that racial factors may be impor

USES AND DANGERS OF CHLORPROMAZINE

Two further uses for that versatile chlorpromazine, have been described Tilley and B claim that in 3 cases of neurodermatitis it consider relieved pruritus and motor overactivity Friedgood Ripstein [6] gave chlorpromazine to 8 drug addicts abrupt withdrawal of their drug (morphine in 5 insta pethidine in 2, and pentobarbitone in 1) No p experienced withdrawal symptoms, and the for the drug of addiction was abolished

It is not surprising that chlorpromazine, which wide range of activity, should exert toxic effects A hypotension is not uncommon, especially when the p is allowed to remain on his feet during the initial of treatment with large doses, and deaths have resu from this complication [7] Several cases of jaundice also been reported,[8–10] and this complication too been fatal The jaundice is peculiar in usually appe to the clinician to be obstructive, biopsy spec have shown intrahepatic biliary stasis [9] or per cellular infiltration [10] Blood changes occasionally ar notably eosinophilia,[9] though agranulocytosis has recorded [11 12] and in 1 case this was fatal [11] These other possible hazards of chlorpromazine therapy sh prompt the clinician to examine critically in every the indications for administering the drug Repea exposure has led to severe dermatitis in nurses [13]

Sir **RUSSELL BRAIN** has been re-elected president of Royal College of Physicians of London for the co year

IN the Cabinet changes announced last week **CHARLES HILL** was appointed Postmaster-General

Prof **EVELYN SPRAWSON**, consulting dental to the London Hospital, died on April 6 while atte a meeting of the council of the Medical Prote Society He was 74 years of age

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[1] Cruice J M *Amer J med Sci* 1914 **147**, 720
[2] C [illegible] A Gibson J R., Webb, W M *Ann intern Med* 251
[3] Choremis, C V, Ninlos N *Acta paediat Stockh* 1949, **37**,
[4] Melville I D *Brit med J* 1951, i 1187
[5] Tilley, R F Barry H *New Engl J Med* 1955, **252** 229
[6] Friedgood C E Ripstein C B *Ibid* p 230
[7] Rea E L, Shea, E J, Fazekas J F *J Amer med Ass* 1 156 1249
[8] Boardman R H *Brit med J* 1954 ii 578
[9] Van Ommen R A Brown, C H *J Amer med Ass* 1955, 321
[10] Zatuchni J, Miller, G *New Engl J Med* 1954 **251**, 1003
[11] Boleman A P *J Amer med Ass* 1955, **157**, 364
[12] Lomas, J *Brit med J* 1954 ii 358
[13] Lewis G M. Sauricky, H H *J Amer med Ass* 1955, **157**,

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Special Articles

AN EXPERIMENT IN
PROPHYLACTIC PSYCHIATRY IN CHILDREN'S HOMES

W LINDESAY NEUSTATTER
M.D B.Sc. Lond. M.R.C.P
YSICIAN IN PSYCHOLOGICAL MEDICINE ROYAL NORTHERN
SPITAL, LONDON CONSULTING PSYCHIATRIST THE L.C.C.
SCHOOL HEALTH SERVICE [1]

THIS paper describes what has so far been done wards creating a prophylactic psychiatric service in e residential establishments of the London County uncil. After six years the practical issues have clarified emselves and an account of them may help anyone io is contemplating, or might contemplate a similar heme

The L C C has 6 residential schools for deprived ildren accommodating about 2500 children of both xes, and 8 small family homes for 200 There are also nurseries and nursery schools, 4 approved schools, 6 hools for the educationally subnormal, 5 schools for e maladjusted (with another 3 opening shortly) 12 hools for the physically handicapped 2 schools for the nd, 2 schools for the deaf and 7 short stay schools for e delicate. This gives a grand total of 5380 children its care in various residential establishments and in dition there are 2 reception homes and one reception ntre with a total annual turnover of 650 [2]

Most of these children are in the council's establish ents because of home circumstances—e.g parental ness divorce, or neglect Hence there is an especially olific field for psychiatric disorders Also although is nominally a specific handicap such as intellectual tardation or organic disorder which is responsible for mission to residential schools for the educationally bnormal or the physically handicapped, in fact the ild is not infrequently in such a school because of home cumstances or an element of maladjustment Thus all idential establishments contain children some of whom least are maladjusted.

The National Health Service is concerned with pro- ling specialist therapeutic services, based on hospitals eatment being their concern the L C C set up what y hope will become a prophylactic psychiatric service part of their public health activities To this end they ve appointed psychiatrists to advise the staffs of resi ntial establishments on child psychology in general. is does not preclude—and, incidentally inevitably led —advising on individual children but formal treat nt of individual cases is considered to be a responsibility the N H S Any children needing such treatment are ferred to child guidance clinics or hospitals

The first step in establishing the new service was my pointment in 1947 as a part-time consulting psychi rist The duties were then largely advising on the ucture of the service so as to pave the way for its work 1949 a full time psychiatrist the late Dr H G illiams, was appointed and on the experience gained e service was later enlarged by appointing three more rt time psychiatrists whose sessions were together ual to those of one whole time psychiatrist In addition r whole time psychiatric social workers have been pointed mainly based on the maladjusted schools an ential duty which they undertake is preparation of e home for the return of the child

At Bredinghurst Maladjusted School a lay psycho erapist is employed for 11 sessions per week In 1948 Mr H A T Child was appointed senior educational psychologist and advises on technical educational problems

THE PSYCHIATRIST'S RELATIONSHIP WITH THE STAFF OF ESTABLISHMENTS

The first step in a scheme of this kind is the acceptance of a psychiatrist by the staff, for psychiatrists are by no means always persona grata They are viewed, at best with suspicion and when besides being psychiatrists they descend from County Hall the reaction to them is distinctly guarded. My first task therefore in 1947 was to try to overcome this resistance Here a psychiatrist's training in listening proved valuable, and at initial visits I did little more than listen One's reception was always friendly enough, and a measure of receding suspicion was the production of time honoured stories about ' trick-cyclists ' Next there would come heartfelt and understandable complaints of the inordinate time it took to get a child to a distant clinic or the interminable waits there—of a member of the staff being thus occupied all day " and then they see the child for a quarter of an hour and send a report telling us what we told them ! "

At this stage the headmaster usually observed how glad he was to have a psychiatrist visit ' only I fear you won't find enough cases here to make it worth your while doctor " This last remark needed to be accepted with some caution Almost in the same breath one headmaster (now retired) pointed to a small boy passing the window and said : He might interest you doctor he has twice tried to set the place on fire ! " A study of the headmaster's psychology is valuable and a tactful reference to the merits of Hutton or Graveney if the headmaster comes from the appropriate county can establish better relationships than many a dissertation on psychology It is very important to try to overcome the common suspicion of the psychiatrist some of which is understandable Those with years of first hand experience of youngsters are naturally apt to resent intrusion of someone who they feel is trying to teach them their job and in dealing with behaviour problems teachers and house staff undoubtedly have practical experience of handling children which psychiatrists lack I have been impressed by the very good understanding of problem children which some of them have shown On the other hand some staff feel that they have a knowledge of maladjustment and child psychology which they do not in fact possess They are not always as aware as the psychiatrist that the ultra good child may be a more serious problem than the disturbed one Some indeed have closed minds and are quite unreceptive to new ideas

Where specific disorders such as hysteria psychopathy early schizophrenia or epilepsy exist, the psychiatrist obviously knows more about these conditions than the layman and this the staff will readily allow Moreover in my experience if one starts by confining oneself to advice on these medical matters where one's authority is acknowledged one's opinion in other spheres will afterwards be more readily accepted

Williams (1953) and Prince (1953) have emphasised that often it is not formal advice which the staff want so much as moral support Prince points out the importance, in schools for the maladjusted of reassuring teachers that only limited success can be hoped for with their difficult charges and of making them accept philosophically the fact that parents of maladjusted children are ipso facto, neurotic and cannot be expected readily to change their stays

Williams also writes of the need to allow individual members of the staff to abreact by discussing their personal difficulties This relief of their feelings can result in greater tolerance of some of their very difficult charges The changed attitude is the outcome of an emotional and not an intellectual reorientation

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[1] The views expressed in this paper are entirely my own and should not be attributed to the London County Council.

[2] Until recently the L.C.C. was also entirely responsible for their Remand Home psychiatric service Now as with child guidance clinics the L.C.C. supplies the building and ancillary staff only

Cooperation with the visiting school doctor was always attempted With a busy practitioner this could prove difficult, but he receives copies of psychiatric reports

SEEING THE CHILD

Having established contact, the next question was how best to get full value from the psychiatric services It is possible either to confine one's activities to discussion with the teachers, *without* seeing individual children, or to see the children as well I unhesitatingly favour the latter method, on the following grounds

(1) Psychiatry is a highly controversial subject, and, purely theoretical discussion of problems may well increase rather than diminish suspicion of the psychiatrist In any case discussing children's problems in the abstract always leads to questions of how a particular child should be handled To advise without seeing the child can be very misleading, because the teacher's account may differ substantially from what would be one's own impression Even after examination one's advice may be incorrectly interpreted, and to advise theoretically involves additional dangers

(2) The psychiatrist is trained to look below the surface and to understand unusual reactions He should thus be able to give something tangible and useful to the child, even though the interview is not primarily therapeutic

(3) Not seeing the child tends further to separate psychiatry from general medicine If a child has a bad heart the doctor is expected to examine him, not to give a dissertation on cardiology The same should hold good for a psychological disorder

Thus I have always made a point of seeing the child, and so have my colleagues This does not preclude discussion in general terms of points of interest with the teachers, and, as one is not treating the children, such discussion is particularly important Indeed, I have given a number of formal lectures which have led to quite a lively discussion, but have also inevitably led my being shown children who the staff feel exhibit some of the traits referred to

I have preferred to give descriptive talks in non-technical language on the "medical" aspects of psychiatry referred to above, rather than embark on psychopathology There is enough in the former to a interest and lead to discussion on different psycho types, while it avoids the opposition and incredul which the more complex expositions of psychopath are apt to be met, the simpler aspects of the b —e g, boastfulness being an overcompensatio feelings of inferiority—are sufficiently well recog nowadays not to need formal presentation

NUMERICAL SUMMARY OF FINDINGS

The accompanying table is founded on returns by the various psychiatrists over a period of a The figures refer to the number of children seen with various disturbances noted, on each occasion If the same child was seen repeatedly it was entered time, and the figures therefore exaggerate the a number of children of one type seen in the year

As the returns were made for administrative pur and not for research, the terms used were unfortuna not standardised, and it is evident that different t were used to express the same disorder, thus be disorder and maladjustment seem to have been synonymously so often that I have felt justified in the two together as "total disturbed behaviour" W several different descriptive terms had been used ("backward and aggressive") it was hard to know w one to choose I took the first one, which may weighted certain of the findings Thus in smaller backwardness was a noticeable feature, yet as often due to anxiety, it could have been tabulated as

In some cases behaviour disturbances were su into more detailed categories, but exact numbers fallacious because everyone did not use these terms in column 1 (physically handicapped) the numbers so small that the percentages must be viewed with caution

It will be seen that disturbed behaviour was b the commonest cause of referral, presumably attracts attention most readily Backwardness nervousness come next most frequently, the figures not sufficiently accurate to show valid co between the groups

SUMMARY OF FINDINGS OVER 12 MONTHS

Type of problem	Types of Institution					
No of children seen individually	Physical handicap 15	Maladjusted school 187	Approved school 42	E S N school 33	Residential school 131	Nursery nursery sch 232
Behaviour problems						
Generally difficult	27 %	55 %	17 %	30 %	48 %	53%
Absconding	0	5 %	5 %	2 %	0	0
Rebelliousness	0	6 %	2 %	0	1 %	0
Temper tantrums	0	3 %	0	2 %	0	1%
Stealing	0	18 %	7 %	2 %	3 %	1%
Minor delinquencies	0	1 %	3 %	0	4 %	1%
"Maladjustment"	15 %	All in theory	30 %	15 %	22 %	7%
Total disturbed behaviour	42 %	88 %	64 %	51 %	78 %	63%
Anxiety reactions						
General nervousness	1 %	12 %	2 %	15 %	2 %	1%
Stammering	0	0	0	0	1 %	1%
Enuresis	0	2 %	0	8 %	2 %	6%
Prepsychotic behaviour	0	0	2 %	11 %	1 %	0
Psychopathy	0	0	0	4 %	1 %	0
Backwardness	20 %	0	7 %	4 %	8 %	23%
Brain damage	15 %	2 %	0	0	0	1%
Epileptic personality	0	0	2 %	4 %	1 %	1%
Subject to sexual assault	0	0	7 %	4 %	1 %	0
Homosexuality	0	0	10 %	0	0	0
Inferiority due to psychical handicap	20 %	0	0	0	0	0
No of sessions spent at each type of school	11	173	20	17	82	97
No of such schools visited by L C C psychiatrists	3	4	2*	5	6	15
Average no per type of school	3 6	43	10*	3 2	13 5	6 5
Average no of children seen per	≏ 1 5	≏ 1	≏ 2	≏ 2	≏ 1 5	≏ 2 5

d school had only an annual visit because of distance another was not visited by our psychiatrist and there were no re
were only approximate, and do not add to exactly 100

Kinds of School

RESIDENTIAL SCHOOLS FOR DEPRIVED CHILDREN

The length of stay in these is determined by outside cumstances, and is not as in 'special' schools for fects, dependent on the response of the child. This ates special problems, because the children may have acclimatise to continuous boarding-school life. One of great difficulties is the large numbers (sometimes to 50 children) in one house which prevents house rents from giving the children the amount of individual ention they would like to give, and which the children ed Also with so many charges they may under ndably find it hard always to show the necessary tience with children of difficult habits, such as enuresis As always, the exceptionally sensitive child whose aladaptation is not obvious tends to be overlooked. erefore the child most needing psychiatric attention often not recognised nor is it easy for the over rdened house-mother to give it the considerable time eeded when it is. The psychiatrist's task is to try to ntify these children and find the best way of securing e special handling they need—a task which is not easy e real solution is outside medical hands since it involves oney, bricks and mortar, and personnel suitable for ese extremely arduous duties

APPROVED SCHOOLS

Apart from the difficulties arising from the high oportion of boys of inadequate intelligence one of e chief problems met in approved schools is the esence of a small number of 'abnormal' offenders ost children in approved schools are not deep psycho gical problems their offences are more readily plained as commonplace reactions to temptation and d influence But in some the delinquency appears more a form of neurotic behaviour—an unconscious expres n of conflict, as in hysteria or compulsive acts The actions of the former are straightforward they are at would be expected particularly in not very intelli nt children or those of weak personality who have ccumbed to bad environment Such types respond to stable atmosphere and to a regular routine and disci ne but the latter often need a freer atmosphere in ich to work out underlying feelings of guilt and hos ty It can be seen therefore that their correct handling an ordinary approved school is very difficult Making ceptions for a few children in a large school leads to vious difficulties

The recognition of children who have been wrongly ced is clearly a function of the visiting psychiatrist. no means all of them need moving elsewhere for itable steps can be taken within the school if the child's ndamental attitude can be gauged The child who els anxious or inferior may have put on a brave face fore the staff but is willing to reveal the true state of fairs to the psychiatrist He in turn can pass the formation on to the staff In one such instance, where boy was very unhappy and had come from a bad me I was able to advise the headmaster who promptly troduced the boy to his dog which proved most effective erapy

Homosexual problems though not peculiar to approved hools are prone to occur in any residential establish ent where the sexes are segregated There is no ready ade or easy solution; but the psychiatrist can do uch to allay the anxiety of the headmasters who el such happenings in their schools may lay them open criticism, and can help the staff to keep the problem perspective

Where cases of sexual practice have arisen I always ink it best for the school doctor or the psychiatrist ther than the teachers to take the matter up with the y Treatment especially when intelligence is low is likely to succeed and the best practical expedient is to send boys with marked homosexual propensities to one school, where the staff have special experience of them and can keep a better watch on their activities.

The value of corporal punishment is a controversial point It is but sparingly used at the approved schools I visit but even the head of a maladjusted school where he has never used it, contended that the right should be there, if only because the substitutes might be subtler and more unpleasant. He felt strongly that it should be left to the teacher's discretion The counter argument is that where the teacher's judgment is good, as with this very headmaster, corporal punishment is not used, but where the teacher's judgment is bad there is a danger that the very boy it may most harm will receive it, because he is the one the teacher least understands Thus at a public school I saw a withdrawn lad who had an L C C scholarship and was proving a complete failure both at work and at fitting in with the others His housemaster remarked that had he not heard he was a "psycho case he "would have beaten him regularly Such an attitude makes "psychos" very dubious about beating being left to the teacher's discretion If, as has been suggested in certain institutions, beating must be sanctioned by the medical officer this puts the doctor in a false position which must interfere with his relationship either with the staff or pupil and abolition would be the best solution But one very real difficulty in avoiding corporal punishment is that so many of these boys have been beaten at home and would fail to understand other methods Incidentally, in regard to the supposed deterrent effect of a good thrashing on delinquency I cannot say whether this has stopped potential delinquents, I can say that I have seen many boys who have been "belted repeatedly at home without any noticeable effect in preventing further transgressions

MALADJUSTED SCHOOLS

Under the 1944 Education Act maladjustment, like educational subnormality or physical handicap is regarded as a disorder requiring treatment by special educational measures In fact, however, its place seems to be rather within the province of psychological medicine and our psychiatrists have accordingly visited these schools not less than once a fortnight and sometimes weekly (see table) There are not more than 50 children in any of these schools and the amount of freedom the children are allowed depends largely on the character of the headmaster

A question of interest is whether formal psychotherapy is needed Some believe there is no need for it in children at all while others think it essential in all cases. In a small experiment on 19 boys at Bredinghurst School by Williams (1953), using improved social relationships and learning capacity as criteria, he found a significant difference favouring the treated versus the untreated group The experiment was open to the usual criticisms of such small surveys involving subjective estimates but is an interesting pointer

Formal psychotherapy apart, in my view a troubled child needs the opportunity to talk about his worries and express his feelings, just as an adult does Contrary to popular supposition this can be done without any need to use complex language to encourage introspection or to make the child feel he is a 'case' Whether such talks are held with a psychiatrist psychologist, or schoolmaster is largely immaterial—except that the latter who may subsequently have to be an impartial disciplinarian is worst placed for the task What matters is that the listener should be objective sympathetic and preferably sufficiently queer himself to understand unusual children—which perhaps puts the psychiatrist ahead of the others! He should also be able to remember enough about his own childhood to see the problem from the child's standpoint This does not necessarily imply agreement or approval, and he may have to explain that it does not But disagreement does not matter provided the child feels that its point of view is being understood and not just overridden

E S N SCHOOLS

At schools for the educationally subnormal the problems are parallel to those in other residential schools, though they are more difficult to deal with on account of the low intelligence of the children When one remembers that child guidance clinics will rarely accept children with an I Q below 70, one realises the difficulties with which these schools have to cope

Children in E S N schools may be maladjusted dullards, whose emotional difficulties have resulted in such an inability to learn that they have had to be dealt with as E S N children, but they are really a variety of maladjustment I have been impressed by the improvement of young unstable E S N children in small residential E S N schools

Occasionally, one sees children who are so emotionally disturbed as to be quite unapproachable and untestable, and have to be ascertained as E S N even though one suspects they are not

An example of this was a pitiful terrified girl of 8 whose mother, a backward unstable woman living with a man, not only knocked the child about but punished her by locking her into a small dark room by herself In the course of a year at a small E S N school, with kindly treatment, she improved considerably, and turned out to be only dull and not E S N

NURSERIES AND NURSERY SCHOOLS

Experience in these has been limited to a year, and willingness to accept the psychiatrist has varied more than in any other establishments The visiting psychiatrist, Dr E Huband, reports that the problems she has met fall into three groups

(1) Fundamentally normal children reacting in a disturbed way *as a result of past bad experiences, or inability to adjust* to nursery routine There, she felt, the psychiatrist could do much by seeing these children and advising on their management

(2) Children who are so abnormal, emotionally or intellectually, that merely *advising is* of limited value Ideally they need different placing

(3) Seriously maladjusted children in need not only of special placing but of actual psychiatric treatment

The outstanding impression has been that visits were too thinly dispersed to make very much progress For the present, policy has switched to seeing the effects of visiting a few of the institutes regularly, and as yet no information is available

PHYSICALLY HANDICAPPED SCHOOLS

The problems met with in children in these schools fell into three groups

First there are psychological difficulties due to an unsatisfactory home situation These are similar to those found elsewhere, but the physical defect is sometimes the cause of parental rejection, particularly if it is disfiguring

Thus a pathetic little girl of 10, with severe congenital heart-disease, was disturbed in her behaviour Her parents mostly lived abroad but even when the mother was in England she never visited the child The child told me she really did not mind as her mother used to call her an ass and a fool when her dyspnœa prevented her tackling a strenuous task.

Secondly, there are cases where feelings of inferiority arise from physical defects, especially where deformity exists

A spastic girl of 12 spontaneously referred to a cardiac case as "lucky" because she looked normal

Sometimes hysteria exaggerates a disability One very int [illegible] girl of 14 was clearly not using her partially [illegible] hand and leg as much as possible, because she preferred to try to ignore her disabilities Again, a child
a marked spinal bifida was incontinent because she
make no effort to go to the lavatory. She, too, seem
prefer to pretend that nothing was wrong

In contrast to these cases, it is gratifying to be ab
record how many of these crippled children I saw
happily in their free time, even quite severely par
boys playing a good game of table tennis

Thirdly there are the cases where physical defect
psychological difficulties are intermingled

For example, a child with kernicterus showed consid
symptoms of anxiety She was always on edge and s
trying to please, almost profusely so She had queer dr
many of which were connected with punishment Sh
dreamt frequently of a boy friend, aged 10, at another s
and of her father kissing her in bed, a thing he had never
She *repeatedly made drawings of animals with curious*
which, she said, were part of somebody's body

One suspected that, in spite of her age, she had co
of a sexual nature She also had lost her favourite brot
Korea Her emotional difficulties probably added
motor instability She would have been an interestin
for play therapy but there were no facilities

It is my impression in all the cases dealt with th
children appreciated the opportunity of discussing
problems with *a doctor, and they seemed to do* so
readily than children in ordinary schools

RECEPTION HOMES AND SHORT STAY HOMES

The psychiatrist has a particularly important r
play in the reception homes, because the need for a
to be received—sometimes very suddenly—into c
itself an indication of a family situation likely to
produced a disturbed child The future welfare
child is very dependent on correct placement, an
task is taken very seriously, usually being settled
conference between the psychiatrist, the psych
social worker, the care committee, and the staff
reception home

In short stay homes, one of the psychiatrist's du
de ascertainment, for quite often children, while
ing placement in a maladjusted school, recover n
through being away from home in a stable environ

Discussion and Conclusions

One of the perturbing questions put by sceptics-
usually resented by psychiatrists because there
reply—is "what proof is there that psychiatric treat
of children yields results, and above all that it pre
later psychiatric disorders?" Figures unfortun
have not proved anything in regard to the latter que
and little in regard to the former, and one has t
back on clinical impressions—an unsatisfactory expe

In the present survey the same difficulties arise
figures given furnish no proof that the psych
services described are in fact preventing future psych
disorders Nor could anything short of an enor
research project *be expected to yield statistical* re
Therefore, one must be content to adduce argum
suggesting that the scheme described here is serv
useful function The following can be said

(1) It seems logical to have a psychiatrist to a
on psychological disorders in the same way that ca
logists or ophthalmologists are employed

(2) The psychiatrist does not exclusively advis
child management as is sometimes supposed His sp
training allows him to recognise certain syndromes—
psychosis, or epileptic disturbances—which the lay
would not recognise As Peter Scott (1953) points
correct sorting of cases is an important functio
psychiatry in the field of delinquency The same ap
to the little-charted seas still to be explored in a se
such as this

(3) The psychiatrist, even at a diagnostic interv
can give the child something tangible in his capa
of an impartial listener unconnected with discip

casionally a child acknowledges this, with a phrase ch as I find it easier to talk to you' This unburdening n be of value.

(4) In such a scheme as this the psychiatrist fulfils the ry important rôle of the doctor in any society he n advise even if he has no specific remedy and he can lieve anxiety In institutions the latter can be of great alue In backing a headmaster where serious offences abnormalities have to be dealt with in giving a acher a chance to unburden himself and in suggestions mere discussions on handling difficult problems, he n take some load off the staff, and this lightening of eir burden is likely to lead to better handling of ifficult children

The whole tenor of modern social services for children to try to avoid the unhappiness with its warping ffects, too often associated with institutions in the past n so far as they achieve this there will be better emotional development for happiness is a most important ngredient in the growth of a healthy mind

Summary

A growing psychiatric service aiming at prevention of uture instability, for children in L C C residential stablishments is described As yet no direct evidence of prophylaxis has emerged or could be expected to have merged, but arguments are adduced that the service dds to the happiness and welfare of the children and hus should assist healthy emotional development

In conclusion acknowledgment should be made to the follow ng for their parts in inaugurating and running this service Dr Leonard Browne alderman of the L C C Sir Allen Daley then M O H and Dr A. W Petrie adviser in mental health, at the start of the service; and Dr J A Scott, present M.O.H for the county of London. I wish to thank the latter for permission to publish the material contained in this paper, and all those who have coöperated in this experiment too numerous to mention individually

REFERENCES

Prince J S. (1953) Personal communication
Scott P (1953) Pamphlet of the Howard League for Penal Reform
Williams H G (1953) Report to L.C.C. Education Committee

HEALTH IN SCOTLAND IN 1954

'THERE is no simple and satisfactory explanation of the fact that better disease control saving of life and improved environment are still accompanied by heavy sickness incidence' With this provocative statement the report of the Department of Health for Scotland[1] sums up the situation in 1954

On the credit side there were fewer deaths in child birth and from tuberculosis than ever previously recorded, as well as a continued improvement in the death rate among pre-school children Nevertheless the incidence of sickness, measured by visits to hospitals and to doctors remained heavy During the year there were more than 2 million new hospital outpatients outpatient attendances totalled nearly 7 million, and nearly 500 000 inpatients were discharged.

A disquieting feature is the persistent rise in the death rate among men aged 50–64 In men aged 55–64 deaths from respiratory cancer in 1950–52 were six times as common as in 1931 coronary thrombosis was six and a half times as common and bronchitis had increased by nearly a quarter (The death rate among females on the other hand, was in all age-groups lower than twenty years ago)

This urgent demand on the curative services has been partly met by expanding the hospital accommodation and by enlarging the hospital staffs By the end of 1954 the number of staffed beds had been increased by 9% over the figure for 1948 the number of hospital nurses had risen from 19 000 to 24 000; there had been an appreciable rise in the number of consultants and senior hospital medical officers; and the annual running cost of the hospital and specialist services had increased from £24 6 million in 1949–50 to £30 2 million in 1953–54 Even so, these increases were small compared with the increase in the number of patients passing through the hospitals

As regards the future, the report is optimistic, expressing the view that the massive amount of work now bein done by the health services will in the long run, prov valuable 'in forestalling the development of seriou disease and preventing the onset of complications.' Ultimately therefore, there will be evidence of reduction in this burden of sickness and of continuin advancement in general standards of physical health an well being'

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[1] Reports of the Department of Health for Scotland and the Scottish Health Services Council 1954 Pp 148 4s 6d

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The Widdicombe File

XXIV THE CLOUDED CRYSTAL BALL

DEAR WHIDDON

I liked your nephew Whatever branch of our profession he chooses, he has some natural advantages He i sound in wind and limb he has done his military servic and avoided marriage he answers questions diffidentl but explicitly his nails and collar are clean His wis to become a pathologist is not as for some of us, a secon choice forced upon him by the fear that he will no succeed in some other preferred way of life Until abou six months ago in Singapore he had no clear idea of wha he wanted to do One afternoon—a time he usuall devoted to repose—his familiar guided his feet to th laboratory and prompted a brother officer to invite hi to look down a microscope I would like to think that th fable of Ross was repeated—that the sight of a malari parasite in all its beauty was the occasion of somethin akin to revelation which pointed out the path of h future life At any rate the laboratory became a habit he learned a little, and he was told that a living might b made that way

I do not see him in academic life His intellectu ability is no more than average and his training in pu science up to a bare pass standard I may be wron Perhaps he will find a secluded niche where he ma learn more and more about less and less ad infinitum. hope not for there are few of our colleagues so much t be pitied as the professors *manqués* too old to sack an too inert to go But I did my best to impress upon hi the value of starting his career in some humble appoint ment in a university department Having to instruc others who know only a little less than he does will teac him his pathological A B C better than anything els If he does not know or cannot find he will be surround by polymaths who can resolve his doubts There will b a library, and if he is lucky a few feet of bench whi he may call his own Above all, he will live in an enviro ment where the main purpose of existence is the enlarg ment of human knowledge (although few of the inmat would like to admit it)

A year or two in this rarefied atmosphere may tax hi stamina but it should leave him something more than craftsman in his trade and with a better idea of what h wants to do

I suggested that he will probably become a clinical pathologist and as I began to expand upon the charms of the life which has kept me from starvation for twenty five years, I was like a Victorian clergyman stricken by DOUBT For to tell the truth I have been thinking for some time that clinical pathology as I know it today is a dying trade It is after all, a hodgepodge of activities which have only this in common—they are done at the laboratory bench If one stroke of the Presidenti pen were to strike off the Register all clinic you surgeons would be inconvenienced nature of your practice would be unch lesser breeds without the law manage to muddle along without our help, and their bills of mortality do not suggest that the effect on medicine is disastrous

When I began, I was the one and only assistant to Diogenes, and we were helped by a man and a boy We "did blood-counts", we cut up the dead, without much understanding we made simple biochemical estimations The work grew, went on growing, and continues to grow—with two results The last of my colleagues who are equally learned (or ignorant) in hæmatology, biochemistry, bacteriology, and morbid anatomy is on the verge of retirement The modern laboratory is a more or less integrated clutter of specialised departments The other result of our trade boom has been the lavish engagement of technical staff until they outnumber the doctors by five or more to one These are, moreover, of a quality outside our dreams of twenty five years ago Unless they present some evidence of higher education we will not look at them Their own examinations are stiff almost beyond reason and a B SC or two among our staff is no matter of note Are you surprised that the counting of red cells and other such chores which used to adsorb nine-tenths of our time are now done almost entirely by the technicians? Helped by better methods and mechanical devices they do them as well as ever we did and a good deal faster

How much use can be made of this galaxy of talent depends, I think, less upon us pathologists than upon you and your colleagues in the wards If you wish to know the level of molybdenum in a patient's blood—I have had dafter requests than this—the problem is a purely technical one There can be only one answer, expressed in microgrammes per 100 ml I believe that it is true of most of the problems which reach our departments of biochemistry and hæmatology that if you can frame the right question the technician can give you the correct answer If, however, you are worried about a patient because his urine is green in the morning, red at noon, and blue at eventide—a condition which you have not met before—you will need the help of a pathologist in deciding what investigations are likely to yield useful answers Some of your colleagues will want this help when faced by far simpler problems and some (oh fie) will ask for estimations of whose purpose and meaning they have no understanding at all It is this failure to ask the apposite question in everyday problems which wastes their time and mine

The weakness of the clinical pathologist's position is that medical education is improving and gentlemen with chameleonuria are rare Free from slavish toil but denied responsibility for patients, he finds that he must devote a large part of his time to helping his colleagues to frame their questions and to apply their answers He is, in fact, a sort of intellectual middleman, and that is no job for a man of parts He boosts his Ego by calling himself an interpreter of laboratory findings, but my private fear is that before long he will be looking for a job at an esperanto conference Nine times out of ten your only wish is to know if your patient is anæmic or has a leucocytosis or a raised blood urea You do not have to ask me or anyone else to "interpret" findings such as these—but neither of us showed up very brightly last Thursday on salt balances and ion exchange I comforted myself with the memory that the great and good physician to whom I clerked was never clear about the distinction between blood urea and blood uric acid And now there is a generation of physicians (and even surgeons) who think as lightly of the newer biochemistry as they do of measuring a limb or percussing a chest If these prodigies can ask the questions and apply the answers without assistance, they may be right to hint that the intervention of a pathologist between them and the technician is an old [illegible]ed formality

Now I know that we in Widdicombe are a little on our toes than they are in Hexworthy and Hoec and I believe that I am thought a useful if not an member of the hospital staff But in W C 1 I rank dimwit, and the casual gossip of a junior registr advanced Choktaw to me As medical education fc —some paces behind—the progress of knowledge, ev those doctors who practise round the sources of the will know more and more of the applications of to the art of medicine Less and less often will ther an interpreter, because they "spikka da lingo"

Having said so much I must, as usual, qualify forecast There are things done in the laboratory cannot be delegated to the very best of technician may cut and stain a section perfectly, but Daw report on the histology is a personal statement of o no different in essence from your own judgment at bedside The mental processes involved in assessing evidence on a biological problem are of a different to those needed for the mechanical estimation of defined chemical substance I doubt if the man who not seen quite a lot of the diseased human body, alive well as dead, is likely to be a very useful morbid ist In diagnostic bacteriology, too, there is more and less science than most people think, but of th have spoken before

I am no solitary prophet Some clinical patholo complain already of the "competiton" of technic and perhaps with reason Those in authority do always understand the ways of the laboratory. Th look on it as an automatic machine which, no matt who is in control, returns infallible answers to ev the most foolish questions They have never learnt th a request for an examination is made by one member the medical staff to another—or should be Abetted some of the Faculty, they have been known to favou laboratory with no pathologist in charge The sadd thing about such a place run by an unsupervised tech cian is that the doctors who use it seldom realise wh poor service they receive I think, too, that it wo do no harm if you and your colleagues would impr upon your juniors that a direct approach to the labo tory staff behind the pathologist's back is bad mann But these are only small straws in a fitful breeze So from wishing to limit the technician's field I would pre to extend it as widely as can be When he has learnt that there is to know in it, he will remain a layman, a there is still work in the laboratory for the man who l learned to recognise the infinite and individual varie of human sickness

The question which the clinical pathologist m answer for himself is the use of the leisure afforded by competent technical staff If he chooses to remain interpreter and nothing more, he must realise that it w always be a humble occupation, without responsibilit or great rewards and likely in course of time to becon as archaic as flint-knapping or woad-boiling If he fe himself to be half a physician—as some do—he will well to set himself up as a whole one, with higher degre and beds and a bowler hat There is as much call for specialist in diseases of the blood as for one in diseas of the chest and his time at the bench will not have bee wasted There is a third course open to those who sti dream of their laboratory as an ivory tower (instead the darkest, dampest, and coldest room in the hospita No one thinks seriously that looking for L E cells or doin a W R is pathology both operations are no more tha the eliciting of physical signs beyond the competence of physician Pathology is the mother science upon which the rational practice of medicine is founded and to which her offspring clinical pathology has added much of value (*Pater semper incertus*, as the lawyers say) In my lifetime I have seen the child degraded to be the Cinderella of our profession and, glass slippers being as rare as chameleon rin, the quicker she returns to mother's lap the better he alternative is an embarrassing tumble between the ed and the bench

So I would have your nephew remember that he is efore all things a pathologist When he reaches a respon ible post let him use his technical staff to the limit of heir skills He must remain responsible for their errors nd should not let any report leave the laboratory unseen nd unsigned He will not detect every inaccuracy but e should know enough to recognise improbabilities If is colleagues seek his advice let him give it freely as a age and not as a phlebotomist hired by those too idle o do their own venepunctures But otherwise his day s his own to do as he wills no operating no out patients, no teaching He may spend it writing letters o THE LANCET, or attending meetings (committee cientific, or race); or even in the quiet pursuit of nowledge A nice life

Your nephew has another advantage I hope all selec ion committees remember that anglers are classed with very honest men"—and quite right too

Yours sincerely

HARRY HAWKE

Public Health

Hygiene in Food Establishments

In a report on the health of Luton in 1954 the borough's chief sanitary inspector Mr G F Macefield, describes an investigation into the efficiency of dish washing processes in public eating places In 29 establishments—such as canteens, school kitchens hotels, and public restaurants—swabs were taken from 308 utensils, mainly plates cups, and beakers 240 swabs yielded fewer than 100 colonies per utensil (the bacteriological standard which, in the United States, is regarded as hygienically satisfactory); 10 yielded 100–200 colonies 5 yielded 300–500 colonies; 10 yielded 500–1000 colonies and 10 yielded more than 1000 colonies. But the report adds that these figures must be considered in con junction with the results from other utensils taken at the same time and on this basis it was found that quite a high standard of hygiene was achieved in the establish ments visited

England and Wales in 1954

The Registrar General publishes this week further details[1] for England and Wales in 1954 some provisional figures had already been given in an earlier return.[2] The estimated total population for the year was 44 480 000, an increase of 100,000 over the estimate for 1953. More people died from accidental poisoning, burns, and falls during the first nine months of 1954 than during the corresponding period of 1953 In the first three quarters of 1954 there were 758 deaths from accidental poisoning (658 in 1953), 621 deaths from accidental burns (522) and 4020 deaths from accidental falls (3327) The number of suicides was 3822, compared with 3512 in the first nine months of 1953 The total number of deaths from respiratory tuberculosis in the whole of 1954 was 7069 compared with 7013 in 1953 Since 1947 the respiratory tuberculosis death rate has fallen by more than 65% The provisional cancer death rate in 1954 was 2222 per million population for men and 1862 per million for women The corresponding figures in 1953 were 2165 and 1835 respectively The rise in the rate for men includes an increase from 607 to 657 per million in deaths assigned to cancer of the lung and bronchus, making a total increase of 70% since 1947

Infectious Diseases in England and Wales

Disease	Week ended March			
	5	12	19	26
Diphtheria	17	9	10	11
Dysentery	1805	1427	1830	1815
Encephalitis				
Infective	2	3		4
Postinfectious	3	3	3	
Food-poisoning	111	181	121	118
Measles excluding rubella	26 453	25 437	29 135	28 682
Meningococcal infection	32	52	48	41
Ophthalmia neonatorum	37	25	33	46
Paratyphoid fever	5	8	7	4
Pneumonia, primary or influenzal	955	963	983	984
Poliomyelitis				
Paralytic	11	9	10	8
Non-paralytic	3	2	3	4
Puerperal pyrexia	235	252	264	247
Scarlet fever	948	782	842	816
Smallpox				
Tuberculosis				
Respiratory	710	693	692	646
Meninges and C.N.S	16	15	9	13
Other	80	96	83	74
Typhoid fever	3		2	2
Whooping-cough	1834	1883	1936	*1867

* Not including late returns

Scotland in 1954

In a preliminary return for 1954 the Registrar-General for Scotland[1] reports that the birth rate continues the rise which began last year At 18·0 per 1000 population the birth rate was 0 2 more than in 1953 The infant-mortality rate was 31 per 1000 live births—the same as last year when the rate reached a new low record The death rate of 12 per 1000 population was 0 5 above the 1953 figure, but 0 3 below the average for 1949–53 The tuberculosis death rates are the lowest ever recorded.

Medicine and the Law

Negligence Action Settled

A Yorkshire miner has been awarded £350 agreed damages in respect of paralysis of the ulnar nerve following an injection in the left arm[2]

The plaintiff aged 50 was admitted to the Castleford Normanton and District Hospital in November 1951 for an operation for perforated peptic ulcer He was put to bed about 8 30 A.M and a male nurse gave him an injection of Omnopon and scopolamine At about 9 A.M. he was taken to an operating theatre and given an injection of thiopentone by the anæsthetist The injection caused him pain and he became unconscious. The operation was performed by a house-surgeon. During the operation it was alleged the surgeon and the anæsthetist were responsible for the care of the patient The plaintiff recovered consciousness at about 5 P.M that day and saw that his left arm, which was painful was tightly bandaged The next day the bandage was removed and he saw that his arm was black and swollen It remained in that condition until he was discharged.

The plaintiff sued the hospital management committee the surgeon the anæsthetist and the male nurse It was alleged that in injecting the thiopentone intravenously the anæsthetist had allowed the drug to penetrate into the surrounding tissues of the arm; that the bandage was applied too tightly that the defendants failed to observe the swelling of the arm and to slacken the bandage at the first opportunity; and that the arm during the operation was allowed to lie in such a position on the table as to cause the paralysis.

Evidence was given by a general practitioner whose patient the plaintiff had been for a number of years that there was nothing wrong with the patient's arm and that he had never had any trouble with it

During the trial a settlement was reached, damages being awarded against the management committee and the anæsthetist and the plaintiff withdrawing the allegations against the surgeon and the male nurse

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[1] Registrar-General's Quarterly Return, no 424 H.M Stationery Office Pp. 35 2s. Registrar-General's Weekly Return, no 13 1955 H.M Stationery Office 1s

[2] See Lancet Jan. 29 1955 p 249

[1] Quarterly Return of the Registrar-General, Scotland for the Quarter ended Dec 31 1954 H.M Stationery Office Pp 40 2s 6d

[2] Yorkshire Post March 29 April 2 1955

Parliament

Health and Welfare of Non-industrial Workers

IN the House of Commons on April 1, Mr HAROLD DAVIES moved the second reading of a private member's Bill to implement the recommendations of the Gowers' Committee on conditions of work among non-industrial workers Since the report of this committee was published at the beginning of 1949, the Government had made promise after promise, and now they had the opportunity to act 12 million people working in agriculture, on the railways, in shops and offices, cinemas and theatres, in the catering trades, and as dental mechanics were unprotected by statutory minimum standards The Bill laid down standards for their health, welfare, and safety

Mr HEATHCOAT AMORY, Minister of Agriculture, agreed that the absence of a statutory code for non-industrial employment was an unjustifiable gap in our protective legislation Since the Gowers Committee reported, however, the Government departments concerned had translated many of their recommendations into concrete proposals which had been circulated to interested organisations as a basis for discussion and future legislation A vast amount of comment on these proposals had been given detailed consideration The Government were in entire agreement with the general object of the Bill, but in their opinion this subject was much too wide and complex to be dealt with properly by a private member's bill Any legislation which was introduced not only must be fair to all parties, but must be capable of effective enforcement Time could not be found in the remainder of the present session to do justice to such an important measure But the Government had already made it clear that it was their intention to introduce legislation of broadly the same scope as soon as parliamentary time could be found

QUESTION TIME

Recruitment of Dentists

Replying to a question, Mr IAIN MACLEOD, the Minister of Health, announced the eleven members of the Interdepartmental Committee, which he has set up, with the Secretary of State for Scotland, to ascertain the reasons for the lack of candidates for training as dentists Sir Arnold McNair, Q C, is to be the chairman and the medical and dental members are Mr J E H Duckworth, Sir Wilfred Fish, Prof A P Thomson, Mr J L Trainer, Mr R O Walker, and Prof F C Wilkinson.

Training of Nurses

Replying to a question, Miss PATRICIA HORNSBY-SMITH, parliamentary secretary to the Ministry of Health, said that the Minister was inviting representatives of the London teaching hospitals to discuss the further secondment of student nurses with his officers next month At Dec 31, 1953, the ratio of beds to nursing staff was 1 27 to 1 in the London teaching hospitals, and 1 79 to 1 in general hospitals under the Metropolitan regional hospital boards

Hospital Pharmacists

Replying to questions, Mr MACLEOD said that he was aware of the shortage of pharmacists in the hospital service In August last there were deficiencies on complements of 281 in the basic grade and 64 in the senior grade There was no nationally agreed salary for hospital pharmacists Payment varied according to the prevailing rate in the area In the Metropolitan area the standard salary of a hospital pharmacist in the basic grade was £450 a year at age 23, rising by annual increments of £25 to £575 with an extra £20 or £30, according to age A claim for salary increases was before the Pharmaceutical Whitley Council It was true that in many cases locums were not as well qualified as the men under whom they must serve, but that by and large they got substantially more than the permanent officers The question whether there should be national rates for locums was a matter that he was sure that the two sides of the Whitley Council would discuss in the negotiations

Group-practice Loans

to a question, Miss HORNSBY-SMITH said that at larch, 1955, in England and Wales, some £36,000 had been paid to eleven partnerships, including 38 as loans for the establishment of group practice

Needs of Elderly Patients in Edinburgh

Mr E G WILLIS asked the Secretary of State for Sco if he was aware that in a recent survey in Edinburgh, 159 doctors of 5086 elderly patients, it was discovered there was a large need for physiotherapy, that some had need of domestic medical assistance and 1270 we need of nursing, hospital treatment or rehabilitation.—C mander T D GALBRAITH replied This survey was cond as part of a joint study, in which Edinburgh Corporation the South Eastern Regional Hospital Board are particip of the needs of elderly patients in Edinburgh The assess of its findings, in particular as to the relative importanc the various needs reported by the general practitioners, matter primarily for these authorities, who will I am take careful note of them in considering the developmen the various services for which they are responsible u statute

Mr WILLIAM ROSS asked the Minister whether, in c quence of the findings of the survey, he would institu national survey into the condition and needs of Scotl chronic sick and old people —Commander GALBRAITH repl Arrangements of varying kinds have been made in diff parts of the country for the joint study by local author hospital boards, and executive councils of the needs to be by their services catering for old people and the chronic But the survey procedure adopted in Edinburgh has not employed elsewhere, and its findings have still to be eval by the bodies concerned

Priority Dental Treatment in Scotland

Replying to a question, Mr JAMES STUART, Secreta State for Scotland, said that in the 12 months to June, it was estimated that expectant and nursing mothers, chil and those under 21 years of age received 198,000 cours dental treatment, or 17% of the total provided unde general dental service In the 12 months to December, the number of such courses was about 650,000, or 57% c total.

Radioactive Content of London Atmosphere

Dr BARNETT STROSS asked the parliamentary secreta the Ministry of Works, as representing the Lord Preside the Council, when measurements were first commence London on the radioactive content of the atmosphere how long such measurements had been taken by the ph department of the Marsden Hospital, and how the techn used there compared with or varied from that used by Medical Research Council —Mr J R BEVINS replied measurements of atmospheric radioactivity in London e than 1947 are known Since that date measuremen radiation backgrounds have been made in the physics de ment of the Royal Marsden Hospital, these are the mea ments made under the auspices of the Medical Res Council Other measurements made in the physics depart since 1930 were designed to ascertain the degree of expos workers using X ray apparatus and radium

Spastic Paralysis and Cerebral Palsy

Replying to questions, Mr JAMES STUART, Secreta State for Scotland, said that compulsory notification hitherto been confined to infectious conditions, and he not think there was enough to be gained to justify a pro to depart from that principle for spastic patients. Me officers of health in Scotland had been asked to includ their annual reports for 1954, statements of inform available about the incidence of spastic paralysis or cer palsy in each area, and to review the facilities available u the local health services for people with this handicap T had also been asked to review the degree to which t facilities were being coördinated with the diagnostic treatment services and with the welfare services When information had been received, he proposed to consider position further

Fluoride Content of Water-supplies

Replying to a question, Mr DUNCAN SANDYS, Ministe Housing and Local Government, said that the officials of Ministry were collecting information about the fluo content of the water supplied by statutory water undertal in England and Wales, beginning with those serving population of more than 100,000

In England Now

Running Commentary by Peripatetic Correspondents

THE newspaper strike, to most a passing inconvenience, has shattered the pattern of my life. It happened like this. For nearly ten years now I've belonged to the best of all clubs—a carriageful of commuters on the 8.8 to Town. There was the bowler-hatted *Times* whom I judged to be a senior Civil Servant; three *Daily Telegraphs*; a fellow who clearly didn't know his own mind, since in the autumn of 1948 he switched from the *Mail* to the *Express*; and a parvenu left-wing newcomer with us only since 1949, who despite our silent disapprobation stuck to the *Herald*. Yet even him we eventually absorbed into the group.

The strike came; and we faced each other, unshielded, for the first time. For several mornings the *Times* opposite me gazed resolutely at Sunny Ilfracombe above my head; and I read above his, How to Get Free Insurance Every Sixth Year. We couldn't go on like that: the mounting tension had to be released. Yesterday morning a stranger got in with the *Manchester Guardian* under his arm, and with oafish mindlessness to the prevailing sense of strain sat down and began to read it. We looked at each other: unanimity was complete. As we handed round the divided sheets a little ripple of talk sprang up and the ripple grew to a torrent. The *Times*, I learnt, was a successful bookmaker who liked to keep himself up with world affairs; while the *Herald* was a Conservative Party official who believed in knowing the enemy. But this bout of chattering was inevitably followed by reaction. As the train drew into the terminus the thaw ended, and we parted with uncertain gestures of farewell, leaving the *Guardian* to gather his scattered pages.

Farewell indeed it was. This morning I got into our accustomed carriage. Only the *Herald* was there, and he hastily hid his face behind the *Spectator*. The others were risking no repetition of yesterday's debauch. I shall miss our silent club. But thank heaven we British have our *standards*—which brook no garrulousness on the 8.8 to Town.

* * *

Whether to tell the doctor is a *complex problem*, but an accepted ethical hazard of being a patient. For instance, *when ill with a high* temperature, pains in the back and limbs, and a headache, you may suggest that you have flu, though there is always the risk that your doctor will bitingly reply that it is his job to make the diagnosis. On the other hand merely to enumerate your symptoms may attract a diagnosis of "*mild pyrexia* with hysterical overlay." The solution is to *know* your doctor and treat him as a whole person with a definite personality and background. *If you are suffering from* vague aches and pains, *not clearly fitting* any described disease, then your problem is more difficult. If you are certain you have a completely new disease, then the more details you can describe the better. Of course your illness will be called after the doctor, unless your name is Easter, Whitsun, or August, and the publication of your illness occurs at the topical bank holiday; but that is really a small loss for having a real illness. If you are not so lucky as to have a new disease, then beware! Study your doctor and decide whether you need medicine or sympathy. If the former, then stress the dominant pain and keep quiet about the others; if the latter throw out some hints about pressure of work, hard-hearted parents, bureaucracy, and Civil Servants (always a winner). Don't tell him straight away that it's your nerves, but let him tell you, and don't, whatever you do, follow up his diagnosis by asking "which nerve?"; remember only the doctor may make such jokes; for the patient to do so shows a blunting of affect and shallowness of emotion. The doctor will reassure you that though he agrees that your pain is really there, it isn't really. You may well leave him muttering:

As I was going up the stair
I had a pain that wasn't there;
It wasn't there again today;
I wish my pain would go away.

* * *

I was listening the other day to the long, sad story of an unwanted child, and of her ill treatment by her parents, the world in general, and her fellow patients—which had precipitated the present crisis—when my somnolence and dutiful yes, yeses were rudely shattered. Striking her most dramatic pose she sobbed: "Oh! I wish I were dead! Oh! Doctor! Give me Oblivion."

Covering my confusion with a gentle "now! now!," I thought of warning Sister, calling psychiatric aid, and delivering a little homily dissociating myself from the recently expressed view of certain management committeemen. But I was saved further mental exertion when she remarked: "A friend of mine recommended it and said she had found it wonderful." I hurriedly agreed and joined her in a quick drachmstat.

* * *

Our small Canadian hospital is trying to organise itself to meet the requirements of the Joint Commission on Accreditation of Hospitals, an august body with headquarters in Chicago. The medical staff is enforcing the following formalities on itself.

Patients' histories must be written within 48 hours of admission, before any *operation is performed*, and on a standard form with a terrifying check list of all imaginable signs, symptoms, and possible previous illnesses. These are checked by the *records committee* which is composed of three members of the medical staff.

A *tissues committee* checks the operation done by the surgeon with the preoperative diagnosis and the pathologist's report on the operation specimen. The question was raised at one staff meeting as to who checked *the pathologist*, but after a slight pause this blasphemy was skated over.

A Gallup poll has apparently established norms of permitted *medical naughtiness*. For instance, you are permitted to remove up to 15% of tissue later reported normal pathologically; to have up to 1% of patients die in the first ten postoperative days; to have a maternal death rate of up to 0·25% and a neonatal death rate of up to 2%. But anything over the norm is held to be *distinctly fishy and in need of* investigation.

A *credentials committee* assesses the qualifications of staff members and suggests promotion or demotion.

As our staff, like the hospital, is small, almost every doctor is on at least one committee. *Consequently* Dr X on the tissues committee cannot be too uppity with Dr Y (whose appendix was reported by the pathologist to be normal, though in the middle of the night before operation it appeared clinically so acute) because Dr X knows full well that Dr Y is on the records committee and Dr X has been rather slack with his histories. Justice therefore tends to be tempered with mercy. I think we shall manage all right; being doctors we know only too well the fallibility of medicine as a science.

* * *

He was a curious character—long haired, pedantic of speech, and in his middle thirties. Once an antique dealer, he was now odd-job *man in a doss* house. He had had attacks of acute pulmonary œdema and he had murmurs in his heart about which the experts found it hard to *agree*, *so that* he was a *difficult* case to teach upon. However, he seemed to enjoy the class and corrected his student's history several times. As we left his bed after much discussion he said: "Excuse me Sir, but if I may make one further observation, I suggest that my murmurs are neither systolic nor diastolic, but apostolic."

* * *

I see as I go round the town
How one goes up and one goes down;
How brother clasps the hand of brother
And how they knife at one another.

A beech tree standing in a glade
Smothers its offspring with its shade;
The little beeches scarce will thrive
While the ancient beech remains alive.

Day by day and hour by hour
Strength vies with strength and power with power
To urge on us and every nation
A thermonuclear termination.

This isn't the whole of the truth about man,
So think up the rest of it if you can.

Letters to the Editor

PREPARATION FOR WAR

SIR,—Though hardly anybody anywhere wants a third world war, we see a continuing increase in preparations for war, with a progressive accumulation of power to destroy life The preparations made by each opposing group are regarded by the other as a threat to life and liberty, but governments are not averse from engendering fear, because they believe it will deter their opponents from aggression The world's governments are acting, in fact, as though they believed that the increase of fear is in the interest of peace It is, of course, just possible that this belief will be eventually justified—that, when all countries have enough reason to be frightened of war they will prefer some lesser risk On the other hand it is quite certain that the immediate effect of fear is to induce nations to amass more arms With very few exceptions, students of human motivation believe that fear facilitates the outbreak of war, and that peace is more likely to be gained by diminishing fear than by increasing it

From childhood onwards we all go through a series of crises in which a choice has to be made between (1) facing and accepting facts, however unwelcome, and (2) trying to dominate the situation for our own purposes In biological terms, our problem is to know how far we can adapt our environment to ourselves, and how far we must adapt ourselves to our environment Complete subjugation of the world to one's wishes is possible only in fantasy the attempt to enforce it in reality, by sheer force of will or by loudness or plaintiveness of demand, is effective only in the special circumstances of the child At the same time, complete submission of the self to the demands of others is neither necessary nor desirable Success is attained mainly by adapting ourselves to the needs of others and so influencing them to help us

From childhood onwards we learn the great truth that people, like things, have to be understood before they can be controlled Any attempt to convert an enemy into a friend needs courage there must always be some risk that he will attack as soon as one has lowered one's defences But the major difficulties are not our justifiable fears so much as our self-deceptions, which trap us into trying to triumph completely, as in a world of infantile omnipotence, rather than to achieve mutual understanding and constructive mutual surrender in the world of reality

It is convenient, for mental comfort, to believe that those who conform to one's wishes are good, while those who seem to frustrate them are bad Moreover, if men can make themselves believe—as they can and do—that the majority of the good people are on their own side of the curtain, while the majority of bad people are on the other, conflict is more effectively externalised On both sides people need someone on whom to project their own antisocial wish to dominate their neighbours, of which they themselves disapprove, and thus each side performs for the other the comforting service of scapegoat But the price of such self deception is incalculable What can we really expect from the mutual fanning of suspicion, fear, and hatred?

London W 1 J NORMAN GLAISTER

GENETIC EFFECTS OF THERMONUCLEAR EXPLOSIONS

SIR,—I wish it were possible to share Dr Carter's optimism, in his letter last week, about the possible genetic effects of experimental thermonuclear explosions in peace time, but his expectations regarding "the eugenic counter measures which mankind will surely take" are nothing more than wishful thinking of the most type It is regrettably plain to anyone with much experience of human affairs that in c even uneasy peace eugenic strivings will be defe religious or conscientious scruples, by basic urges, and even by a sort of sheer cussedness which defy the advice of the Eugenics Society precisely it is the advice of such an organisation! If world nuclear war should break out perhaps these sc be overcome or over ruled, but it is doubtful w organised government will persist in such a form a be able to apply eugenic principles in time The one can hope is that a few people, at the end of time, will have started practical fumblings toward Dr Carter would like to see

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Two things, however, are known that genetic dam is irreversible and that a considerable part of the r active material liberated by these explosions remains, all intents and purposes, permanently active It fol that by the time human observation shows that danger point has been reached the damage will have b done and nothing will undo it Common prudence w suggest, therefore, that experimental explosions sho cease until such time as investigations have provide little more information as to what level of radiation be regarded as safe In spite of the difficulties involved in extrapolation, two or three years of intelligently pla laboratory experiment ought to give some inte approximate result and might indicate a permis rate at which the physicists might continue to let off the fireworks

Some highly reputable physicists have already sa that the next stages in the development of nucl weapons can be carried on without test explosion Politically, therefore, a suspension of explosions wh intensive genetic research goes on is feasible and sa Medically and eugenically it is hard to see why a doctor should hesitate to press for such a suspension.

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THE DOCTOR, HIS PATIENT, AND THE ILLNESS

SIR,—I read with great interest Dr Balint's article of April 2 Most of us have met the patient who needs a "bad" doctor, but I, as a consultant, only met him once

It was one of my earliest consultations An elderly man came to me complaining of hairy black tongue I had seen the condition in dogs, but though I knew it occurred in man, I had never met it I inquired about diet and I found that he ed largely on bread and meat and was therefore flatulent l constipated.

He handed me two sheets of foolscap on which were cata ued the opinions and advice of 17 leading skin specialists England, France, and Germany and with great joy he d me they were no use at all Though not a leading specialist was considered worthy to contribute my scalp

I advised him to eat more vegetables and fruit and to have raviolet light (new in those days when there were no amin B preparations) His black tongue vanished at once d he never forgave me His cherished symptom and his t of bad doctors were his *raison d être* and reverting to his i ways, he did not live very long for which he was thankful believe.

Bitton, near Bristol. A T TODD

CLINICAL STAGING OF CARCINOMA OF THE BREAST

SIR,—I should like to be allowed to add a footnote Mr Michael Harmer's letter of March 26

There is associated with this department which is sponsible for statistical analysis of data relating to ses of cancer registered in England and Wales, a ommittee under the chairmanship of Dr A H T obb-Smith which advises on cancer statistics generally d on the national registration scheme in particular t recent meetings this committee, which is a sub ommittee of the Registrar General s Medical Advisory ommittee (chairman, Sir Ernest Rock Carling), has en much concerned with the problem of establishing niform systems of staging Largely for the reasons numerated by Mr Harmer it has selected the breast s the most suitable site for immediate study In doing is, the committee is of course taking account of arious existing methods of staging including those onsidered at the sixth congress of the International nion against Cancer

General Register Office
London, W.C 2. R M BLAIKLEY

BURNS FROM ELECTRIC BLANKET

SIR,—Dr Neville Davis (April 2) writes about a child ho received a shock from an electric blanket which had ecome wet with urine The danger is from using electric lankets heated directly from the mains By far the afest plan is to have a blanket taking its current at a oltage not greater than, say, 20 from the output side a mains transformer Suitable transformers can be ought new made up to specification, or obtained second and. The transformer should have an output of about 00 watts the secondary side should be tapped to give 0 volts and 6 volts. The cost of a new transformer is bout £4 and a second hand one about 35s

An electric blanket measuring 4 ft 6 in. × 5 ft. (suitable for double bed) can be made up from two bed sheets or any imilar material between which is threaded 45 yards of plastic overed bell wire (outside diameter 1 mm) obtainable from Woolworths at 1½*d* per yard The wire is threaded back ards and forwards across the sheets and the sheets machined etween each turn and around the edges; the two ends of the wire are brought out of one corner

The transformer should be mounted in a good strong box he mains side wired in three-core rubber cable and properly arthed. The secondary side should be switched to give the utput either from 20 volts (high) or 6 volts (low); this side may be earthed to the frame of the transformer The transformer box is placed near the head end of the bed and the blanket plugged into a 2 amp. socket with a two pin plug

On a bitter cold night the bed will be warmed up to luxury omfort in about twenty minutes when switched on high If then switched to low and left it will be very pleasant ll night On a less cold night it can be switched off altogether when about to go to sleep

The blanket is absolutely safe There is no danger from shock through passing urine in the bed or spilling water when washing or bathing an invalid The blanket can be made at home for about £1 The transformer can be mounted in a box and wired also at home if father is a competent craftsman, or it can be done outside for about £5 The total cost is about £6 as against about £12 charged for mains voltage electric blankets We have had one in our house throughout this past winter; the comfort of it is wonderful

Twickenham Middlesex. J MADDISON

SURGERY IN HÆMOPHILIA

SIR,—Dr Walker's most interesting and full report (April 9) of gastrectomy in a hæmophiliac undoubtedly succeeds in its main object—that of underlining the extreme risk of surgery in hæmophilia however mild Even minor operations should be avoided in these patients whenever possible, and only carried out under cover of transfusion and with full laboratory control Major surgery should be resorted to only if it provides the one hope for the patient s survival.

Exchange transfusion as carried out in Dr Walker's patient, affords the best preoperative preparation at present generally available In view of the admitted instability of antihæmophilic globulin in vivo as well as in vitro however operation should be performed as soon as the exchange is completed. It is probable that Dr Walker's patient would have required less blood and plasma postoperatively had the gastrectomy been performed immediately after the exchange transfusion instead of twenty hours later

St. Thomas's Hospital
London S.E 1 R M HARDISTY

THE ACTION OF CHLORPROMAZINE

SIR—I am glad that Professor Samson Wright (April 2) is prepared to suspend judgment on the unconventional explanations offered by French authorities In fairness to them I feel I must point out that it is difficult to set out in a brief review the results of twenty years research by a team of full time workers and it is possible I have not done full justice either to their experimental methods or their explanation of their findings. Furthermore the fact that their work is little known in Anglo-Saxon countries is explained in part by their isolation during the German occupation of France and in part by their reluctance to publish their failures to achieve a satisfactory method of preventing the development of their syndrome

In 1935 O Shaughnessy and Slome[1] came to rather similar conclusions after their work which showed the effectiveness of spinal anæsthesia in preventing the development of traumatic shock in cats After noting the ineffectiveness of attempts to compensate for fluid loss by intravenous therapy they stated

> "Up to the present, apart from perfunctory administration of morphia too little attention has been paid to the nervous side The body possesses ample reserves of fluid and the shocked case who recovers does so because he has been able to replenish a diminished volume by drawing on natural resources. We have suggestive evidence that it is the continuance of abnormal impulses which prevents this natural reaction on the part of the organism and if these impulses can be controlled this favourable reaction takes place Some better method of controlling nociceptive impulses may be devised—but control in some form is essential for the successful treatment of this syndrome.

Over 50 years ago George Crile reached rather similar conclusions on which he based his anoci association and kinetic theories of shock. Present-day opinion seems to agree about the specificity of the reactions of the organism to non specific aggression or 'stress, although attention in this country and America seems to have been directed towards endocrine activity to supply the explanation In spite of this little significant progress has been made with endocrine extracts in the prevention of the evolution of these syndromes

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[1] O'Shaughnessy L., Slome D *Brit J Surg* 1935 22, 617

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Two things, however, are known that genetic damage is irreversible and that a considerable part of the radio active material liberated by these explosions remains, to all intents and purposes, permanently active It follows that by the time human observation shows that the danger point has been reached the damage will have been done and nothing will undo it Common prudence would suggest, therefore, that experimental explosions should cease until such time as investigations have provided a little more information as to what level of radiation can be regarded as safe In spite of the difficulties involved in extrapolation, two or three years of intelligently planned laboratory experiment ought to give some interim approximate result and might indicate a permissible rate at which the physicists might continue to let off their fireworks

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Bitton, near Bristol. A. T TODD

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General Register Office
London W.C.2
R M BLAIKLEY

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An electric blanket measuring 4 ft 6 in. × 5 ft. (suitable for a double bed) can be made up from two bed sheets or any similar material between which is threaded 45 yards of plastic covered bell wire (outside diameter 1 mm) obtainable from Woolworths at 1½*d* per yard. The wire is threaded backwards and forwards across the sheets and the sheets machined between each turn and around the edges the two ends of the wire are brought out of one corner

The transformer should be mounted in a good strong box the mains side wired in three-core rubber cable and properly earthed. The secondary side should be switched to give the output either from 20 volts (high) or 6 volts (low); this side may be earthed to the frame of the transformer The transformer box is placed near the head end of the bed and the blanket plugged into a 2 amp. socket with a two pin plug

On a bitter cold night the bed will be warmed up to luxury comfort in about twenty minutes when switched on high If then switched to low and left it will be very pleasant all night On a less cold night it can be switched off altogether when about to go to sleep

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St. Thomas s Hospital
London S E 1
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In 1935 *O Shaughnessy and Slome*[1] *came to rather* similar conclusions after their work which showed the effectiveness of spinal anæsthesia in preventing the development of traumatic shock in cats After noting the ineffectiveness of attempts to compensate for fluid loss by intravenous therapy they stated

> Up to the present, apart from perfunctory administration of morphia too little attention has been paid to the nervous side The body possesses ample reserves of fluid and the shocked case who recovers does so because he has been able to replenish a diminished volume by drawing on natural resources. We have suggestive evidence that it is the continuance of abnormal impulses which prevents this natural reaction on the part of the organism and if these impulses can be controlled this favourable reaction takes place Some better method of controlling nociceptive impulses may be devised—but control in some form is essential for the successful treatment of this syndrome

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[1] O'Shaughnessy L. Slome D *Brit J Surg* 1935 22 617

Letters to the Editor

PREPARATION FOR WAR

SIR,—Though hardly anybody anywhere wants a third world war, we see a continuing increase in preparations for war, with a progressive accumulation of power to destroy life The preparations made by each opposing group are regarded by the other as a threat to life and liberty , but governments are not averse from engendering fear, because they believe it will deter their opponents from aggression The world's governments are acting, in fact, as though they believed that the increase of fear is in the interest of peace It is, of course, just possible that this belief will be eventually justified—that, when all countries have enough reason to be frightened of war they will prefer some lesser risk On the other hand it is quite certain that the immediate effect of fear is to induce nations to amass more arms With very few exceptions, students of human motivation believe that fear facilitates the outbreak of war, and that peace is more likely to be gained by diminishing fear than by increasing it

From childhood onwards we all go through a series of crises in which a choice has to be made between (1) facing and accepting facts, however unwelcome, and (2) trying to dominate the situation for our own purposes In biological terms, our problem is to know how far we can adapt our environment to ourselves, and how far we must adapt ourselves to our environment Complete subjugation of the world to one's wishes is possible only in fantasy the attempt to enforce it in reality, by sheer force of will or by loudness or plaintiveness of demand, is effective only in the special circumstances of the child At the same time, complete submission of the self to the demands of others is neither necessary nor desirable Success is attained mainly by adapting ourselves to the needs of others and so influencing them to help us.

From childhood onwards we learn the great truth that people, like things, have to be understood before they can be controlled Any attempt to convert an enemy into a friend needs courage there must always be some risk that he will attack as soon as one has lowered one's defences But the major difficulties are not our justifiable fears so much as our self-deceptions, which trap us into trying to triumph completely, as in a world of infantile omnipotence, rather than to achieve mutual understanding and constructive mutual surrender in the world of reality

It is convenient, for mental comfort, to believe that those who conform to one's wishes are good, while those who seem to frustrate them are bad Moreover, if men can make themselves believe—as they can and do—that the majority of the good people are on their own side of the curtain, while the majority of bad people are on the other, conflict is more effectively externalised On both sides people need someone on whom to project their own antisocial wish to dominate their neighbours, of which they themselves disapprove , and thus each side performs for the other the comforting service of scapegoat But the price of such self-deception is incalculable What can we really expect from the mutual fanning of suspicion, fear, and hatred ?

London, W 1 J NORMAN GLAISTER

GENETIC EFFECTS OF THERMONUCLEAR EXPLOSIONS

SIR,—I wish it were possible to share Dr Carter's optimism, in his letter last week, about the possible genetic effects of experimental thermonuclear explosions in peace time, but his expectations regarding "the eugenic counter measures which mankind will surely " are nothing more than wishful thinking of the most alistic type It is regrettably plain to anyone with much experience of human affairs that in cond even uneasy peace eugenic strivings will be def religious or conscientious scruples, by basic urges, and even by a sort of sheer cussedness w defy the advice of the Eugenics Society precisely it is the advice of such an organisation ! If w nuclear war should break out perhaps these scru be overcome or over-ruled, but it is doubtful organised government will persist in such a fo be able to apply eugenic principles in time T one can hope is that a few people, at the end time, will have started practical fumblings tow Dr Carter would like to see

With the more optimistic among the scientist that the tolerance of human genes to radiation times greater than the present level of bac radiation, but it is possible that in fact huma achieved only a marginal adjustment and that over, say, a doubling of the present sea level might be dangerous We do not know and cann until a good deal more research has been carried

Two things, however, are known that genetic is irreversible and that a considerable part of th active material liberated by these explosions rem all intents and purposes, permanently active I that by the time human observation shows danger point has been reached the damage will h done and nothing will undo it Common pruden suggest, therefore, that experimental explosion cease until such time as investigations have pr little more information as to what level of radia be regarded as safe In spite of the difficulties inv extrapolation, two or three years of intelligently laboratory experiment ought to give some approximate result and might indicate a pe rate at which the physicists might continue to let fireworks

Some highly reputable physicists have alrea that the next stages in the development of weapons can be carried on without test ex Politically, therefore, a suspension of explosio intensive genetic research goes on is feasible a Medically and eugenically it is hard to see w doctor should hesitate to press for such a suspe

Public Health Department,
Colchester JOHN D KERS

SIR,—Why does Dr Carter consider desira maintenance of the human species in its normal lished genetic pattern ? To what end does mankind "is prepared to undertake control of evolution," or to what purpose does he think "will surely take" eugenic counter measures "irreversible genetic deterioration" ? What does he see ahead ?

As a second question, may I ask him whet "methods of achieving highly selective reprod would be applied as a dictate of intelligent (a planning, or as the inevitable (and not freely result of mankind's instinct for self preservatio the former, again may I ask what is the aim of th If the latter, I wonder if this instinct itself is gen typed and likely to be influenced by mutations

Holt, Norfolk J N COZENS HA

THE DOCTOR, HIS PATIENT, AND T ILLNESS

SIR,—I read with great interest Dr Balint's of April 2 Most of us have met the patient wh a "bad" doctor, but I, as a consultant, only m once

It was one of my earliest consultations An elde came to me complaining of hairy black tongue I h the condition in dogs, but though I knew it occurred I had never met it I inquired about diet and I found ved largely on bread and meat and was therefore flatulent nd constipated.

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[1] O'Shaughnessy L., Slome D *Brit J Surg* 1935 22, 617

It would appear, therefore, that neurogenic theories deserve re consideration, and it is hoped that Professor Samson Wright's restrained and open-minded attitude will encourage further study of French ideas in this country and America

Lambeth Hospital,
London S E 11

D A BUXTON HOPKIN

IRON-DEXTRAN COMPLEX IN MICE AND MEN

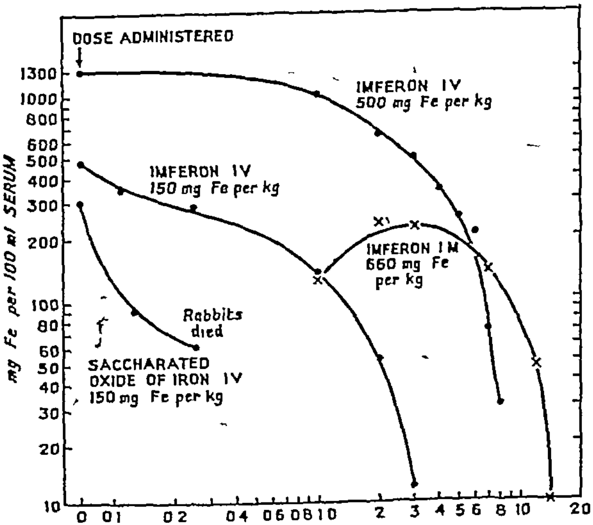
SIR,—We feel that certain comments are called for by the interesting observations reported by Dr Nissim in your issue of April 2 The administration of the iron-dextran complex 'Imferon' to mice in doses which provided 500 mg of metallic iron per kg of body-weight, *with survival of the animals*, was only possible because of the exceptionally low acute and chronic toxicity of this complex Such large doses permit a degree of experimental siderosis never hitherto achieved They are therefore of interest in relation to hæmochromatosis, post transfusion hæmosiderosis, and nutritional cytosiderosis

It should be emphasised, however, that doses of this magnitude bear no relation to even the greatest degree of therapeutic excess The usual *total* dose in man is 20 mg per kg, and in any event is unlikely to exceed 50 mg per kg As Dr Nissim has pointed out[1] in connection with intravenous saccharated iron oxide

> "The doses required for the production of lesions in the rat and mouse are not less than 1 0 g Fe/kg given over a period of 3 months This corresponds to 60 g Fe for a 60 kg adult, and would require some 50 courses of treatment in a case wrongly diagnosed as iron deficiency anæmia"

In Dr Nissim's experiments with imferon the maximum dose was increased up to 3 g Fe per kg over a period of six weeks or less—in animals which were neither anæmic nor depleted of their body-iron reserves

In the ordinary course of pharmacological testing of imferon its acute and chronic toxicity were studied Within the limits of dosage applicable to man, with a wide margin of safety, no depression of spermatogenesis was observed in mice and rabbits Single doses in mice ranged from 100 to 1375 mg Fe per kg intravenously The animals were killed six days later and the iron deposition in the testes was found to vary from a few granules in occasional interstitial cells (at the lower dose) to heavy infiltration associated with fluid staining blue by Perles's method (higher doses) In the rabbit a dose of 650 mg Fe per kg intramuscularly revealed



only a scanty retention of iron in the int
of the testes six weeks later In no insta
evidence that spermatogenesis was in any
The statement that the deposition of iron
following imferon is "more massive than
organ in the body" presumably refers to
iron after eleven weeks, since the initial
is of course heaviest in liver and spleen

The significance of the difference betweer
and saccharated oxide of iron becomes evid
compares serum iron decay curves (see
figure) Whereas the greater part of the
oxide leaves the circulation within the fi
after intravenous administration, imferon
days and so results in the blue staining f
by Dr Nissim The suggestion that a sm
size is responsible is not borne out by our ol
the iron content of peritoneal fluid after th
administration of the two forms of iron
doses of 200 mg Fe per kg The values we
per 100 ml) 'Ferrivenin' 0 374, imferon
ferric ammonium citrate Dr Nissim gives
and 7 5 following doses of 180 mg Fe p
urinary iron excretion of imferon and ferr
the same order—namely 1%, in contrast
ferric ammonium citrate

Research Department
Benger Laboratories Ltd
Holmes Chapel Cheshire

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W
L I

VENEREOLOGY AND DERMATO

SIR,—I have read with much interest Colon
letter of Feb 5, and, with due respect to his
position and judgment, I am not sure that h
to the problem as we have it today

In general, I would suggest that there is n
a good dermatologist should not at the san
good venereologist I am quite convinced
venereologist should be a good general physi
I think he should be able to teach the physicia
above the management and treatment of
cardiovascular syphilis

I have found that it is a very valuable ass
gynæcologist and a dermatologist working in
diseases clinic and taking regular sessions the
large towns and the smaller towns are, I an
different propositions

There is no doubt that the incidence of vene
has fallen enormously in the past few year
still plenty of work to be done in the large t
towns of about 50,000 inhabitants there is n
work to justify many sessions per week It is
of time and money for a consultant vene
attend several 2 or 3 hour sessions per we
average attendance of perhaps 6 or fewer
session in all, and less than 1 new patient p

I am quite convinced that proper faciliti
be given in every town of any size for the t
venereal diseases, and I am also quite sure
will depend upon the enthusiasm and intelli
medical officer concerned

The ideal is, of course, that a V D clinic sho
all day and every day, but again that is quit
able in the smaller towns

I do not believe that Colonel Harrison's s
an occasional visit by a consultant venereolog
works well in practice I admit that the sol
staff problem is difficult, but I suggest that
logist in the smaller towns might well b
venereologist and part time, say, physician, de
or pathologist

In my view, with the decline in venereal d
to the advantage of the medical officer to hav

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[1] Nissim, J A *J Path Bact* 1953, 66 185

[2] Nissim, J A *Brit J Pharmacol* 1953, 8

tring to his bow, and the success or failure of a particular linic will largely depend upon the individual appointed e should preferably be attached to the local hospital nd should advertise (!) his specialty to his colleagues in he hospital and surrounding area

Birmingham and
Midland Eye Hospital.
ERIC W ASSINDER

DANGER OF VITAMIN-K ANALOGUES TO NEWBORN

SIR,—In connection with Dr Allison's disquieting observations on the hæmolytic effect of 'Synkavit' in premature infants (March 20), we have carried out studies, during the past year, on the effect of water soluble vitamin K substitutes on rats On the suggestion of Dr Allison intramuscular injections of synkavit were made, at the level of 10 mg per 100 g body weight into rats deprived for long periods of vitamin E Within a few hours most of the animals became listless or appeared uncomfortable, and an intense hæmoglobinuria ensued Except in a few cases the immediate injury was temporary and both the animals and their urine appeared normal on the following day

Hæmoglobinuria was never observed after injections of synkavit into normally nourished rats or into rats given a basal diet deficient in vitamin E but with adequate supplements of tocopherol When administered orally, synkavit appeared to be harmless even to rats deficient in vitamin E Injections of an aqueous preparation of vitamin K_1 were also harmless to such animals. Preliminary trials with vitamin K substitutes other than synkavit have indicated wide variations in their degree of toxicity, some appearing completely innocuous but others much more toxic than synkavit on a weight-for weight basis

Dunn Nutritional Laboratory,
University of Cambridge and
Medical Research Council
T MOORE
I M SHARMAN

SIR,—Dr Allison's views on the possible dangers of he administration of vitamin K analogues to premature nfants are of great interest. Recent experience in the Derby premature baby unit may perhaps lend clinical upport to these views

The routine care of all babies in this unit was modified recently and the dose of water-soluble vitamin K ynkavit) was increased from 10 mg once on admis on to 10 mg t.d.s. for three days. To my dismay hortly after the introduction of this routine six babies eveloped clinical signs of kernicterus and subsequently ied between the ages of 6 and 13 days. Their birth eights ranged from 2 lb 6 oz to 4 lb 7 oz. Blood investi ations did not show any evidence of rhesus or other lood-group abnormality At necropsy Dr G R Osborn ound typical yellow staining of the basal ganglia

It seems possible that the increased dose of vitamin K ontributed to the kernicterus in these babies, though bviously the condition may have arisen quite fortui ously

This was a most unpleasant experience but I hope Sir, hat others may consider and comment on the implica ions of Dr Allison's findings and this clinical report

Derby
BERNARD LAURANCE

PROTECTING THE MOTORIST

SIR,—In your leading article of Feb 26 you refer to arious ways of increasing the motorist's safety

I gave up a convertible (drop head) coupé and bought sedan (saloon) to secure the strength of steel should the ar overturn Next I purchased a pair of safety belts for he front seat While the central belts are anchored to he floor on either side of the shaft the lateral belts are astened by plates and screws to the rear edges of the ront doors (our doors are hinged at the front) As a result he more the doors tend to open in a crash the more securely one is held in place The belts are of the airplane type and are easily opened

You suggest that such belts might be uncomfortable, but I am very happy with them. Because one is held securely there is not the fatigue of spinal flexors and extensors constantly contracting and relaxing to maintain posture Unlike the airplane seat (deep and enclosed'), the motor-car seat—at least in American cars—is not of the bucket variety, and there is thus no sense of cramping as in airplanes I agree that a harness would be better—one large company of car makers is said to be planning its manufacture

Both in Congress and in various State legislatures Bills have been introduced to make obligatory the installation of safety belts in new cars

Department of Pathology
St. Joseph Hospital Fort Wayne 2,
Indiana U.S A
S M RABSON

RUPTURE OF LAPAROTOMY WOUNDS

SIR,—During the last eight years like Mr Mills (March 20), I have used continuous nylon sutures for the repair of abdominal wounds and hernias; but, while I agree that this reduces to a minimum the risk of rupture of the wounds or of development of hernias, it does have some disadvantages.

The main disadvantage is the risk of infection and sinus formation, and if the method is used routinely then I think this complication is likely to occur more frequently than Mr Mills suggests In my units I have been very satisfied with this method of suturing in the case of hernias, but when it was being used in the repair of laparotomy wounds the incidence of sinus formation and the need to remove the nylon made us decide that it was not suitable in every case

Once infection starts it carries on until all the nylon is removed It is useless to delay removing the nylon or to try the effect of antibiotics The wound has to be opened up the nylon removed in its entirety and the wound lightly packed with tulle gras or similar dressing To be content with removing only part of the nylon or partly resuturing the wound after removing it, inevitably results in failure to heal. One of the disappointing features is that wounds that have apparently healed perfectly by first intention sometimes break down months afterwards

While sinus formation is the main disadvantage there are two other minor complications. A few patients complain that their wound feels tight and they do not seem to be able to stretch presumably due to the inelasticity of the nylon suture and an even commoner complaint is that the knot forms a lump often tender under the skin

There is no doubt that sinus formation does represent a failure in asepsis, and I have come to the conclusion that it is not a suitable technique for standard use in a busy teaching hospital in the dirty atmosphere of a city with the theatre full of students and many of the operations being performed by registrars. But I have continued to use it routinely when working under nearly perfect conditions in an air-controlled theatre outside the town, with a minimum of persons in the theatre and only one abdominal operation being done at a time Under these conditions I have had only two cases of wound infection in the last eight years.

I have found that no 7 nylon is rather stiff to use, feels lumpy under the skin—especially in thin patients—and the knots are frequently prominent and painful I prefer a 44 inch length of no 5 black nylon doubled, and the ends knotted With the double length there is no question of the needle coming unthreaded as it so often does with a single length When the suture is completed one width of nylon is cut, the final stitch is inserted and then the two ends are tied. This makes for a smaller knot, and the first and last stitches can easily be inserted so as to make the ends turn in to the deeper tissues

Liverpool
J B OLDHAM

BEHÇET'S SYNDROME

SIR,—The paper by Dr Phillips and Dr Scott (Feb 19) has attracted a great deal of attention The article, however, illustrates one of the main dangers of eponymous description It is not true that Behçet's syndrome "has seldom been recorded in this country" Under a large variety of titles many papers have been written about it in England and America A fuller bibliography was given by me in a paper which I wrote over 14 years ago,[1] and since then there has been an extensive literature on the subject

I myself have seen over a hundred cases of associated recurrent vaginal and oral ulceration, and in almost all of these patients the ulceration occurred with a definite relationship to menstruation—hence the title of my article was Cyclical Mucosal Ulceration None of my cases had eye lesions, but do they therefore belong to a different nosological group ? As I pointed out in that article, there is no doubt that many single girls suffer with this condition but do not report the vaginal ulceration to their doctors, often because of false modesty

Eight young women doctors who suffer from this condition have consulted me about treatment, and all of them have informed me that they know many people who are also afflicted The great majority of the large number of patients whom I have seen have been single women The marital state of their patients is not mentioned by Dr Phillips and Dr Scott

I have also seen over 30 cases of recurrent buccal ulceration in young men, none of whom had either eye or genital lesions But surely these cases also belong to the same syndrome, call it what you will

London, W 1 M H PAPPWORTH

A BARBITURATE ANTAGONIST

SIR,—The case reported by Dr Montuschi and Dr Wickenden (March 19), coupled with Dr Harris's paper (Jan 22), prompts me to report a recent experience with β,β- methyl ethyl-gluterimide (NP 13) in the treatment of barbiturate poisoning

An obese woman, aged 53, swallowed phenobarbitone gr 72 at 3 30 P.M on March 11, and was admitted to hospital at 5 P M. She was then deeply comatose and completely flaccid and areflexic, with small non reacting pupils, blood-pressure 90/60 mm Hg, pulse rate 60 per min , and respiration-rate 20 per min Barbiturate was found in the stomach washings Penicillin was administered, and physiotherapy, with repeated laryngeal suction, was carried out throughout the illness The patient was fed by an intragastric drip, and a self retaining catheter was inserted into the bladder At 9 15 P M the patient responded to severely painful stimuli but otherwise her condition was unchanged Barbiturates were not detected in the urine

On the fourth day after admission pneumonia developed and extensive adventitious sounds appeared in the chest , the temperature rose to 100 8°F, the pulse rate to 116, and the respiration rate to 36 This infection gradually resolved On the fifth day (March 15) the deep tendon reflexes returned, and the cough and swallowing reflexes were clearly present Mild hypokalæmia (serum potassium 3 3 m eq per litre) developed, which responded to increased intragastric potassium. The urine contained a large amount of barbiturate

On March 16 some deterioration was obvious and the deep reflexes were absent At 8 P M NP 13 240 mg was administered intravenously over 90 minutes ('Daptazole ' was not available) There was some transient deepening of the respirations but no other change On March 17 the patient was somewhat less comatose , the reflexes were again easily elicited, and tests for urinary barbiturates were weakly positive It was decided not to administer a further dose of the drug, because of her improved condition Coma gradually decreased, and by the evening of March 21 the patient was fully conscious

It is obvious, in view of the account by Dr Montuschi and Dr. Wickenden, that the absence of clinical improvement in this instance was due to insufficient d but I felt that caution should be exercised in ad ing this relatively unknown drug

I wish to thank Dr C E Kellott, under whose patient was admitted, for permission to publish th and also Dr N A Wynn, of the department of phy King's College, for his interest and for supplying the

General Hospital
Newcastle upon Tyne MORGAN MCELLI

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[1] Brit med J 1941, i, 271

GENERAL PRACTITIONERS' HOLIDAY

SIR,—Consultants in the National Health Serv entitled to six weeks' holiday per year During th they are not obliged to find a deputy, or if they one they are not obliged to pay him

No such consideration has been given to the h of the general practitioner, who, if he takes one has to find and pay a locum Consequently, un can get a partner or colleague to do his work f he may not get much of a holiday And why partners or colleagues be called upon to do this when they usually have quite enough to do alread

As there are many unemployed doctors in the c could not the Ministry form a pool, and allow practitioners to call on it for locums—the M paying the fees ? This arrangement would all general practitioner to have a well-deserved holiday of six weeks like his consultant coll Or the six weeks could be limited to senior practit while the junior practitioners and the junior cons could have four weeks

Littlehampton,
Sussex HUGH STEW

HOSPITAL STAFFS

SIR,—It is not clear what Dr Dickinson (Mar seeks to gain by adding further irrelevancies to an tangled problem His basic fallacy is the assu that the pay of junior hospital staff and the c difficulties experienced by senior registrars in obt consultant posts are in some way related On the con the number of senior registrars (which is the crux problem) is determined not by their salaries, w over liberal or otherwise, but by such factors needs of the hospital service, the number of consul in-training judged appropriate to the specialty, ar financial capacity of the National Health Servic reduction in the pay of registrars, up to a point, only have the effect of diminishing the *initial fi* candidates for ultimate consultant status and cr a bias in favour of those who have private mea who are prepared either to forgo marriage or to and live on their wives There is no evidence tha of these types necessarily make better consu than do more ordinary mortals On the other reducing the pay of registrars beyond a critical leve achieve what Dr Dickinson apparently envisages equanimity—that is, an increasing number of registrarships throughout the hospital service T the matter in the simplest terms two major of the National Health Service at present are (*a*) diffi in obtaining registrars for the less attractive hos and (*b*) a superfluity of candidates for principalshi general practice How then can increasing the bias in favour of general practice redress the balance

Ideally, the pay of the registrar, as of every of the community, should accurately reflect the l and expense of his training, the value of his se the attractiveness of his job, and similar considera Discussion based on such premises can be of real and those who conscientiously believe that are paid more than they are worth are fully entitle state their case (and indeed it may be a good one) let them first make their case, not assume it , and them not then proceed to apply their hypothe problem with which it has at the moment not the motest concern.

I have written throughout in terms of registrars nce it can hardly be argued that an economic deterrent would be used to discourage candidates from applying for house-appointments.

St. Mary's Hospital,
London W 2.

H McC GILES

INACCURACY IN THE LABORATORY

SIR,—Dr Bassir is less than fair to the chemical pathology laboratories in this country in his letter of March 26. He states that only a few laboratories participated in the recent international survey to which your annotation referred and he implies that most biochemists are complacent in the present situation. The facts are that 40 British laboratories took part—a number limited only by the number of samples which it was possible to prepare (a total of 200 for distribution to all the countries concerned). As organiser of the survey, I had to refuse many people who wished to coöperate.

In reply to Dr Bassir's query about the clinical value of extra effort towards accurate results, it is apparent that the interpretation of results is made more difficult by a large observed biological variation. This is made up of two parts: the natural biological variation and the superadded analytical uncertainty. We may be able to do little or nothing about the former, but we should not make matters worse by analyses which are less precise than they should be.

There has also been some progress towards standardisation of methods. For a long time the Association of Clinical Pathologists has issued broadsheets of recommended methods (including chemical analyses), while the Society for Analytical Chemistry has compiled a bibliography of standard methods applicable to chemical pathology.[1] The American Association of Clinical Chemists has recently published volume I of *Standard Methods of Clinical Chemistry*,[2] and further volumes are in preparation. Such publications are, of course, in the nature of recommendations only, and the responsibility for the method used remains with the director of the laboratory. In many circumstances the recommended method may be inappropriate.

The committee which is analysing the freeze-dried samples of serum was jointly constituted by the Association of Clinical Pathologists and the Association of Clinical Biochemists. Its function is to keep the whole subject of chemical laboratory accuracy under review and make recommendations. The secretary is Dr E M Darmady, of the Central Laboratory, Milton Road, Portsmouth.

Postgraduate Medical
School, London W 12

I D P WOOTTON
Secretary, International
Association of Clinical Biochemists.

SIR,—In connection with Dr Jordan's letter of April 9, may I say that prior to the international survey with freeze-dried serum a general invitation was extended to all laboratories by Dr Wootton and Professor King[3] in these terms:

"We intend to look further into the comparability of results obtained in different laboratories both in terms of absolute values and proportionality of results, and to investigate the possibility of some system of regular checks. Any laboratory which is willing to participate is invited to communicate with us."

Area Pathology Laboratory,
Westwood Hospital,
Beverley, Yorks.

O BASSIR

HOLES, KNOBS, AND WIRES

SIR,—There is no doubt that hetero-suggestion and auto-suggestion play a part in determining our attitudes towards works of art. But the forces of suggestion are not peculiar to the world of art (abstract or representational); they are equally influential for our attitudes in all spheres of life—e.g., in politics, morals, religion, and philosophy. However, more worthy of debate is Sir Henry Turner's implication (April 9) that only representational art can give genuine and lasting æsthetic pleasure. He says, for example, that surrealism is faring better than purely abstract art because it "uses recognisable objects." His paper is, in fact, an attack on abstract art in general, *not merely the expression of a personal* dislike for "holes, knobs, and wires."

One does indeed still meet people who seem to believe that unless a painting or sculpture can show a recognisable dog, horse, man, or tree, it cannot possibly yield æsthetic pleasure. All the same it is an undeniable fact that certain (by no means all) combinations of straight and curved lines, dots and dashes, triangles and squares—yes, even holes, knobs, and wires—can produce an effectively pleasing design. It may be "meaningless" in the representational sense; its only meaning is that it gives æsthetic satisfaction, and is not this the sine qua non of art? It is true that much in modern art is atrocious, but this is not because it consists of "meaningless objects," as Sir Henry suggests, but because it is ugly in form, design, and colour.

Park Prewett Hospital,
Basingstoke.

I ATKIN

SIR,—Sir Henry Turner in his analysis of abstract art has unconsciously begged the question—unconsciously because he has not taken into account his own unconscious. Clearly he is an abstract artist without knowing it. Whence did he derive his prescription for his work of art? From his unconscious. This produced the title *Time Passing*, which is to be represented by "three (or more) upholsterer's coiled springs." The spiral is almost too respectable a symbol for time. Note the significance of "three (or more)": this introduces the three dimensions of space, and the "more" indicates their expansion to the four or multi-dimensional space-time continuum. The inverted and illuminated aquarium bowl is a composite symbol of the sky and water into which the creation was first differentiated.

Abstract art, Sir, has scored off Sir Henry! He has designed a work of cosmic significance. *Time Passing* portrays the Universe.

If this interpretation is the result of hypnosis,

I am, &c.

Peckham, S.E.

HYPNOTISED

THE HAIR OF THE PILONIDAL SINUS

SIR,—If a visitor from outer space alighted [illegible] coniferous tree and decided to investigate its origin, he would reason somewhat like this. The pine-tree has stuck in the ground, having arrived from outer space like the visitor himself. In this view the visitor would be fortified when he recalled the frictional forces with which he had to contend during his flight. Did not the branches of the pine tree point in the same direction as the fins of his rocket?

Professor Scarff and Mr Page's picturesque arguments in their letter last week, now based on trauma, now on suction, now on friction, are not supported by factual evidence. In 19[illegible] they wrote [illegible] The [illegible] fact requiring explanation [illegible] required [illegible] pilonidal sinus is why [illegible] stantially in two [illegible] and the appearance of [illegible] tion which they [illegible] made [illegible] by the [illegible] sinuses [illegible] several other [illegible]

Bibliography of Standard, Tentative and Recommended or Recognized Methods of Analysis. Cambridge, 1949.

Reiner, M. Standard Methods of Clinical Chemistry. New York, 1953. Vol. I.

Wootton, I. D. P., King, E. J. *Lancet*, 1953, i, 471.

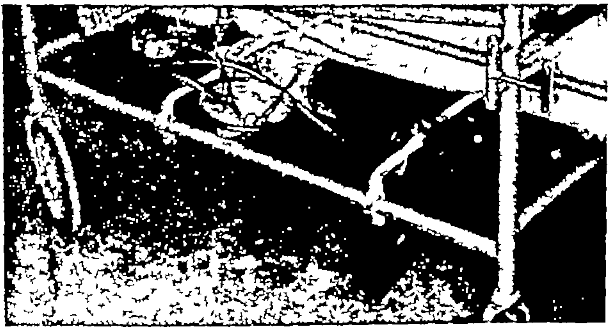
Comparison of hairs in the pilonidal sinus with those in skin follicles reveals that the scales in the latter are more prominent Hence their frictional resistance must be greater If then the frictional forces are as potent as we are led to believe, how does *any* hair ever reach the surface of the skin ? Why does it not just curl up on its papilla and give up in despair ?

We are asked to believe in frictional movements between the sides of the natal cleft, with the best will in the world these are difficult to demonstrate We are asked to confirm the theory by rubbing a hair in our palms, in my hands this does not work And we are asked to believe that the demonstration of hair-bulbs and root-sheaths in the depths of a pilonidal sinus is a freak of mechanics Surely, Sir, to have filled "the one gap in the case for the acquired origin of natal-cleft pilonidal sinuses" few would make bold to claim ?

London S W 10 F E **Wealf**

AN OXYGEN-CYLINDER CARRIER

Sir,—I was interested to see the oxygen cylinder carrier described by Dr Green and Mr Killick[1] A similar attachment has been in use on the *anæsthetic* trolleys at this hospital for about five years There is one useful addition—namely, a carrier for a stainless steel bowl to contain mouth-gag, tongue forceps, and swabs I suggest that manufacturers should consider making these as a standard fitment to all theatre trolleys



Solihull Hospital,
Birmingham.

Harold B Watson

BACKWARD IN READING

Sir,—Having long ago abandoned the mechanistic view of natural processes implicit in medical training for the organismic view, I adopt the same attitude to a reading disability in a child as I do to enuresis

All learning is a growth or maturation process The infant knows how to support his head on his neck and shoulders when, at approximately three months, his posterior neck muscles and the system of nerve with which they are integrated have matured sufficiently He stands walks, buttons his clothes, controls his bladder, and adds two and two when the organisation of brain, muscle, and gland have matured and differentiated to the extent necessary for these organised performances It is literally true that a child grows to read, as it is also true that he grows to control his bladder The rate of maturation of the organisation as a whole will be different in individual children and will also differ in respect of individual lines of development in the same child Experience suggests that the "norm" for bladder control by night is anywhere between a lower limit of three years and an upper of six or seven It is therefore as senseless to bring a child of three to a psychiatrist for "wetting" at night as to seek advice for inability to stand at six months As regards reading, Dundee Research Council found very many years ago that a child was not sufficiently mature to respond to formal phonic instruction in reading until he had reached a mental age of at least seven years

In ten years of child guidance under a local au I have dealt with several hundreds of cases of but I have never seen a case of delayed control th not already been subjected to mechanistic te punishment and reward or formal moralising In cases the child was charged with tensions induced punitive or anxious attitudes and personalities same applies in a modified form to my experi reading "disabilities" Where the previous histo attentively studied it will always be found that th child has been subjected to premature "training"

Perranporth, Cornwall D **Jackson**

APPOINTMENTS IN THE WEST INDIES

Sir,—Recent issues of your journal have cont advertisements for specialist posts in the Col Medical Service (H M Overseas Medical Service many islands of the British West Indies Most of th posts call for specialist qualifications or experi The salary offered is on the average £1500, and may appeal to the person of registrar status ea around £1000–1300 in the United Kingdom, who anxieties as to his future in the National Health Se and may be enticed by the mention of "income at local rates" and by visions of sunshine

The advertisements do not mention the high cost of li in these islands—often as much as 50–75% higher than in U K In certain instances, a housing allowance is pro (maybe £100 p a), but in these cases it is virtually impo to obtain a suitable house for less than £250 p a In s places income tax rises to 7*s* 6*d* in the £ after £800 of tax income, and the allowances are similar to those in the U. Most appointees are rapidly disillusioned on arrival in particular Colony, and a few have cut their losses and retu to the U K. within a short time of arrival

I would strongly recommend intending applic for these posts to inquire carefully into the cost of liv the income tax rates, the housing difficulty, and conditions of local practice If at all possible, should obtain their information from someone on the s

Jamaica
British West Indies

John D Arneau

TREATMENT OF SYPHILIS

Sir,—After your excellent leading article on subject[1] I should like to describe my observation treatment with penicillin of the later stages of la syphilis, and the possible Herxheimer reaction wh as you say, "cannot be prevented or diminished *starting with small doses of penicillin* The reacti of the 'all or none' type"

I administer 1,000,000 units of procaine penicillin G aqueous suspension daily for six days a week for two w and every second day in the third week—a total of 15,00 units of penicillin in three weeks In the first week I com in the same syringe with 1,000,000 units of procaine penicil 50 mg (2 ml) of cortisone acetate suspension ('Cort Merk), and in the second and third weeks 25 mg of suspension

In 87 consecutive cases there has been no Herxhei reaction Cortisone in the doses used does not inte at all with the treponemicidal effect of the penic because 1,000,000 units of procaine penicillin G is n above the minimal effective dose of penicillin my opinion this method helps also to prevent *dysfunction of vital internal organs, and especially o* cardiovascular system in the form of "therap paradox"

Thus, in summary, the combination of penicillin cortisone suspension (in the same syringe) permits treatment, prevents complications, including the H heimer reaction, and, in my view, makes obsolete preliminary administration of bismuth

Toronto, Ontario, Canada L G **Polymenak**

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[1] R A., Killick, F *Lancet*, 1954, ii, 1266

[1] *Lancet*, 1954, ii, 1268

RUPTURE OF THE DUODENAL STUMP AFTER GASTRECTOMY

SIR,—We read with interest the article by Mr Houson in your issue of March 10. We recently treated a case in which obstruction of the afferent loop occurred This obstruction was followed by gangrene of the loop but the duodenal stump remained intact

A man, aged 67 was admitted to the Metropolitan Hospital after a small hæmatemesis. A few hours after admission he had a further severe bleed. He was transfused and about 24 hours after he was first seen a partial gastrectomy of the Polya anti-colic type was done A large bleeding ulcer was found on the lesser curve.

Postoperatively the patient's condition was satisfactory Intermittent gastric suction through an indwelling Ryle's tube was used and bile was aspirated Fluids were given intravenously Oral fluids were started on the second postoperative day and the Ryle's tube was removed next day when his condition was satisfactory Late on this day he vomited and the tube was replaced On the fourth postoperative day he complained of severe abdominal pain which was colicky at times. Only a few millilitres of fluid was aspirated from his stomach and there was no bile in those aspirations. On examination there was no generalised distension but there was tenderness and guarding in the left upper quadrant of the abdomen Bowel sounds were normal By the following day there was a suggestion of a palpable mass in the left upper quadrant

Laparotomy was carried out on the sixth postoperative day An enormously distended loop of small intestine presented on the left side of the abdomen which was first thought to be the efferent loop but after decompression it was seen to be the afferent loop which had passed through the retro-anastomotic gap[1] The loop was gangrenous as far as the duodenojejunal junction and was resected Continuity was established by anastomosing duodenum to distal jejunum The patient died the same day

Post mortem examination confirmed that the duodenal stump was intact and in view of the condition of the bowel it is probable that untreated perforation of the afferent loop would have occurred rather than rupture of the stump

London S.E.26

G M LUNN
C F NOON

TUBERCULIN TESTS

SIR,—After reading your annotation of March 26 I feel more and more confused about the interpretation of a positive test. The W H O call many reactions to 100 T U non-specific you prefer non tuberculous If it can be shown (as I can) that school-children who have reacted to the jelly test (10 T U) (and were radiographed in consequence and thereby shown to have primary tuberculous infection in the thorax) have later failed to react to 100 T U then the W H O statement cannot always be true for these children must have passed through a phase of mild reaction to this concentration I know of a score of such positive X ray/negative Mantoux cases

Again in administering B C G by multiple puncture it was often observed that those pupils who were formerly positive to 10 T U., but who were now non reactive to 100 T U showed an earlier and more definite local vaccination reaction and were quickly rendered allergic—in seven days and sometimes less B C G (intradermal three or four years ago) reverters revaccinated by multiple puncture last week showed local reaction in forty-eight hours and allergy appeared simultaneously How are these phenomena explained if they were originally non tuberculous or non specific?

Regarding the bovine and avian mycobacteria it is interesting to note that only the human organism has been found in lesions in human beings in Lewis since 1940, when special steps were taken to type the organisms recovered from any tuberculous lesion

In 1949 I learned that hens dead of fowl pest had been found to have co-existing tuberculous lesions I tested a dozen hens and found one reactor and in 70 children who had reacted to the jelly test I did comparative Mantoux tests with P P D human and avian using 0·00002 mg Not all the children reacted to both: in 3 cases the erythema at the site of the avian test was somewhat more extensive than on the other arm where the human P P D had been injected

Stornoway
Isle of Lewis.

R STEVENSON DOIG

PARKINSONISM DURING TREATMENT WITH RESERPINE

SIR—As you observe in your leading article of March 12 reserpine the active alkaloid of *Rauwolfia serpentina* is being increasingly used in the treatment of hypertension and of psychiatric disorders[1 2] Clinical reports so far published have commented favourably on its lack of toxic effects. In the following cases, two inpatients receiving large doses of reserpine developed conditions clinically indistinguishable from parkinsonism which disappeared when the drug was discontinued.

CASE 1—A man aged 43 was admitted to hospital for treatment of a moderately severe obsessional and anxiety state which had been intermittently present for four years. On admission he was anxious, tense and mildly depressed and he had obsessional preoccupations with fears of insanity and of death. His blood pressure was 180/90 mm. Hg and he had a fine tremor of the outstretched fingers He improved somewhat after admission, and his residual symptoms were treated by reserpine (0·5 mg b.d for six weeks) During this time his condition changed very little although he put on 6 lb in weight When the reserpine was discontinued however his tension anxiety depression anorexia and obsessional symptoms returned. It was therefore decided to give him 15 mg of reserpine daily After four days he had become much more depressed and anorexic he was very restless, and he had suicidal ideas. He also had a fast coarse tremor of his trunk and limbs. The dose of reserpine was reduced to 7 5 mg daily and two days later his depression had markedly improved He was still restless and the tremor continued though it was less obvious Over the next five days he developed a mask like face and a bowed head on stooping shoulders, he complained of excessive salivation, and he did not swing his right arm on walking There was no rigidity Reserpine was thereupon stopped The tremor disappeared almost immediately and the facial expression became normally mobile within a fortnight but the patient did not swing his right arm freely for about six weeks. The original psychiatric symptoms returned within a week. The blood pressure was unchanged throughout.

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[1] Stammers, F A R. *Brit J Surg* 1934, 22, 11.

doses of reserpine These two cases illustrate one of the toxic effects of larger doses

We are indebted to Dr D L Davies for permission to report these cases and to Ciba Laboratories Ltd for supplies of reserpine in the form of 'Serpasil'

The Maudsley Hospital,
London, S E 5

J S STEAD
J K WING

EFFECT OF ANÆSTHESIA ON FIBRILLATION

SIR,—During an anæsthetic given for prostatectomy to an old man with auricular fibrillation (the anæsthetic including trichlorethylene), his fibrillation became intermittent and then stopped Rhythm, apart from a few extrasystoles, remained regular after 12 days

The patient, who was 79, was fibrillating slowly at about 80 beats a minute, and the blood pressure was around 170/80 mm Hg He had had digitalis folia (gr $^1/_2$ b d) for nine days, with no loading dose Premedication was pethidine (100 mg) and atropine (gr $^1/_{100}$) Thiopentone (0 25 g) and *d* tubocurarine (15 mg) (the latter repeated after cystoscopy) was followed by nitrous oxide, 40% oxygen, and 1–1$^1/_2$% trichlorethylene After 30 minutes, fibrillation became spasmodic (fast and very erratic), and 30 minutes later rhythm was completely normal at 60 a minute Shortly after this atropine gr $^1/_{100}$ raised the pulse to 120, and neostigmine 2$^1/_2$ mg hardly affected this

A patient with fibrillation may return to normal rhythm at any time Trichlorethylene is occasionally recorded as producing fibrillation Digitalis is likely to have been concerned in this case Stress may induce return to normal, and I wonder whether the marked response to atropine may be a hint that this was the main mechanism here

London, E 11

JOHN BARNARD

RABIES IN GERMANY

SIR,—Referring to the fourth reason in Mr Wells's letter of March 26 about why vaccination of dogs in Germany has been rejected, I suppose that some confusion has arisen In Germany the vaccinated dog is considered a source of danger, and this idea rests on the fact that a vaccinated dog is itself protected against clinical symptoms, but it is nevertheless possible that such a dog will secrete infectious saliva if it is contaminated subsequently

The Netherlands report on rabies in Western Germany, discussed in your annotation of Jan 1, has been published in its original form in the *Nederlandsch Tijdschrift voor Geneeskunde* [1]

Staatstoezicht op de Volksgezondheid
Utrecht

G D HEMMES
Rapporteur

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[1] *ijdschr Geneesk* 1954, 98 2421

Appointments

RECK, L S, M B Durh F F A R C S D A consultant anæsthetist Hartlepools and Sedgefield H M C S

AWSON J J Y M C M D Lond M R C P senior consultant chest physician Plymouth clinical area

NEY ROGER M B Lond F R C S T D M R T consultant radiotherapist, regional cancer service Newcastle R H B

LLA THOMAS, M B Edin D P M senior registrar in psychiatry, Bristol Mental Hospitals

YF WILHELMINA N, M R C S D P H school M O, co Durham

AROON SHAUKAT M B Punjab L M D G O registrar in obstetrics and gynæcology Gloucestershire Royal Hospital, Gloucester

LACHLAN, G P M B Edin, D C H, D P H deputy M O H and school M O Exeter

CH HENRY M B Polish School of Medicine Edinburgh M R C P whole time research asst in neuropathology Stoke Park Hospital, Bristol

YNNE MARY A M B Durh school M O co Durham

uth-Eastern Regional Hospital Board (Scotland)

ARMSTRONG H I O, M B Edin F F A R C S D A whole time consultant anæsthetist West Fife group of hospitals

BARD F D, M D Lond deputy senior M O to the board

J A F C S T F R F R F R D M R T consultant radio at radiotherapy department, Royal Infirmary,

Edin, F F R D M R T consultant radio d at radiotherapy department, Royal burgh.

Obituary

ARTHUR FERGUSON MacCALLAN
C B E, M.D Camb, F R C S

As founder and director of the Ophthalmic Hospital of Egypt, and as ophthalmic surgeon to the Westminster Hospital and the Royal Eye Hospital, Mr MacCallan divided his career between two countries But in his particular subject his reputation was far wider, and was president of the International Trachoma Organisation

He was born in 1872, the son of the Rev J Ferguson MacCallan, vicar of New Basford, Notts, and was educated at Charterhouse and Christ's College, Cambridge With a university exhibition he continued his medical studies at St Mary's Hospital, qualified in 1898, and took the F R C S in 1899 For three years he was house-surgeon at the Royal London Ophthalmic Hospital, Moorfields, and then became chief clinical assistant In 1903 his name was suggested to the professor of ophthalmology at Cairo as the most suitable man to organise the new Egyptian ophthalmological service, under the trust established by Sir Ernest Cassel, with the object of conducting a vigorous campaign against trachoma throughout the country On appointment his first step was t study the different phases of trachoma, and he suggeste that this could best be done by observing the children the government primary schools But it was only aft great administrative difficulties that he was allowed 1907 to undertake the treatment of 464 boys in a scho at Tanta. He was so impressed by the importance of th work that he later arranged for all the 70–80 Egypti *doctors to whom he taught ophthalmology to serve* a time at a school, for he held that the treatment *crowds of patients attending a hospital clinic irregula did not give nearly so much insight into the stages of t* disease

Besides training a corps of ophthalmic surgeons fr *among the young Egyptian doctors seconded to him* the department of public health, MacCallan had also set up a chain of provincial hospitals He successfu used ambulatory *hospitals to advertise the need f* permanent hospitals In remote parts he also found more practical to bring the treatment to the *patie* His Cambridge M.D thesis, for which he was *award* the Darwin prize of his college, summed up his experien and described his system of classification by four stag It was published in 1913 as a monograph with the t *Trachoma and its complications in Egypt*

In 1912 by order of Lord Kitchener, then High Co missioner, MacCallan undertook a *survey of the inciden* of ankylostomiasis and bilharziasis in two provinces Egypt, and organised two travelling hospitals to d with these diseases As a result of this work he w *appointed, against his own wishes, head of the epidem* logical section of the department of public health in 19

When war broke out in 1914 he was on leave England, but he was ordered to return at once to Eg by Lord Kitchener In 1915 he reorganised the f ophthalmic hospitals in North Egypt to receive casual from the Gallipoli campaign, he also sent three of travelling ophthalmic hospitals to Ismailia and Suez receive Turkish wounded In 1916 he was *posted* senior medical officer, with the rank of major, R A M at the base at Mersa Matruh on the Mediterranean co *of the Western Desert province*

He returned to civil ophthalmic work in 1917, and 1923 the Egyptian government appointed him direc general of the epidemic services and general hospit but he resigned and returned to London, where he appointed ophthalmic surgeon to Westminster Hos and surgeon to the Royal Eye Hospital

But his interest and influence in Egypt continued, and in 1925 the Memorial Ophthalmic Laboratory at Giza near Cairo, was opened through his efforts as a memorial to the men of the Egyptian labour corps and camel transport corps who had fallen in the war of 1914–18 The original laboratory had been financed by the gifts of MacCallan's personal friends the new laboratory a fine modern building designed by Noel Dawson was planned and equipped internally with MacCallan s expert advice. His former pupils subscribed for a bronze bust of him by Doyle Jones, which was placed in the laboratory and unveiled by the British High Commissioner in 1931 His honours included appointment as O B E. in 1918 and C.B.E. in 1920 and membership of the Turkish Order of the Medjidieh (third class) and the Egyptian Order of the Nile (second class)

MacCallan took a prominent part in the international campaign against blindness, and he was elected president in 1935 of the International Organisation against Trachoma The following year he was given a seat ex officio on the International Council of Ophthalmology and he was re-elected to the presidency up to 1954 when he was elected honorary president for life

When MacCallan joined the staff of Westminster Hospital in 1924 he was nearly 53 years of age with an established reputation in the ophthalmological world

'It must be rare indeed,' writes A. A., ' that a hospital staff is called upon to welcome a newcomer substantially older than the majority of its members, yet MacCallan was rapidly incorporated and thoroughly enjoyed his thirteen years of close association When he retired in 1937 he was appointed consulting ophthalmic surgeon, and during the late war he returned for a period to act as supernumerary Slim with handsome clear-cut features and a placid expression he had an air of distinction to which care in dress and punctilious manners contributed. His diction his vocabulary his mannerisms were of a type—Charterhouse and Victorian Cambridge as a colleague expressed it A poor public speaker he became animated in individual conversation; and though only a few were admitted to his intimacy nobody could fail to recognise a desire to take every opportunity to perform a courtesy and kindness."

Of MacCallan's work in Egypt P D T R writes

"His battle against the trachoma virus was on a heroic ale. His personality was forthright and tireless, selfless, able nd enterprising so that he was ideally suited to driving rough the delays and inertia that had blocked progress in e development of health services in Egypt for centuries ast as founder of a succession of eye hospitals, and as eacher of a devoted *corps of Egyptian oculists he attained* he renown he so fully deserved

"His sense of duty was a constant companion from his arliest days in a Nottinghamshire vicarage to his later service chairman of his local parish council During the late war he eturned to carry the weight of the eye department at Westminster Hospital, then bereft of eye-surgeons, as well as being C.O. to his local Home Guard As a great personality he will e remembered by all who knew him—occasionally with awe or he was intolerant of inefficiency and obstruction but lways with affection and admiration—and by the countless ear blind of the Middle East with deep and well-deserved ratitude

Mr MacCallan married in 1918 Hester McNeil Boyd Carpenter whose father was Bishop of Ripon from 1884 to 1911 She survives him with two sons and a daughter He died on April 1 at the age of 82

Dr G F PETRIE

D W H writes: 'Petrie was by temperament a ecluse so appreciation of him must be restricted to the knowledge obtained in the short but sometimes highly ntertaining intervals when the barriers were down He had at least two qualities which were invaluable in ne so completely devoted to science as he The first as a profound respect for and deep knowledge of the nglish language This gave him a driving urge to imbue he young scientist who came under his direction with ome of his enthusiasm Many of us who have to edit cientific papers are at least now grateful for the memor ble midnight hours of discussion on the best way of xpressing it ' They led, I hope to an indelible improvement in our approach to the compilation and presentation of scientific data His second outstanding attribute was a keen power of observation By chance it did not lead to the fame of a Pasteur or a Fleming, but in this quality he was of their company Diffidence and a seemingly excessive caution might be regarded among his worst enemies He was a keen naturalist with a peculiar leaning for taxonomy With Sir John Ledingham he developed—late in life for a Scot—an ardent interest in golf I am eternally sorry that I missed the privilege of caddying for him. Even one such experience might have led to a much better understanding of his approach not only to the ball but to life He was a product of the Lister Institute, and like all of us who have had that honour, he was devoutly proud of it

Births, Marriages, and Deaths

BIRTHS

BEARN.—On March 30 at New York Hospital New York, to Margaret (née Slocum) wife of Dr A G Bearn—a son.

MOTTRAM.—On April 9 to Kathleen (née Prout) wife of Roy F Mottram M B 47 Croftdown Road London, N W 5—a son (Felix John)

STELL.—On April 9 at Chester, to Dr Eleanor Davies Jones the wife of John Laidman Stell A.T D—a third daughter

MARRIAGES

DAVIS—LIDDLE.—On April 2 at Beverley Minster, Yorkshire Leslie Russell Davis, M B of the Royal Free Hospital London to Margaret Jean Liddle S.R.N of Cottingham Yorkshire

DEATHS

ROCHE.—On April 7 Alfred Reginald Roche M.R.C.S. of 13 North Park Avenue Leeds, aged 79

Diary of the Week

APRIL 17 TO 23

Monday, 18th

MEDICAL SOCIETY OF LONDON 11 Chandos Street, W 1
8.30 P.M Dr J G Scadding: Treatment of Pulmonary Tuberculosis (First Lettsomian lecture)

Tuesday, 19th

ROYAL COLLEGE OF PHYSICIANS OF LONDON, Pall Mall East, S W 1
5 P.M Dr A M. Cooke Aspects of Skeletal Disease (First of two Lumleian lectures)
ROYAL COLLEGE OF SURGEONS OF ENGLAND Lincoln s Inn Fields W C 1
5 P.M. Mr John Foster Idiopathic Stricture of the Valve of Krause (Hunterian lecture.)
ROYAL SOCIETY OF MEDICINE, 1 Wimpole Street W 1
5 P.M *Pædiatrics* Dr Maurice Campbell Dr R E. Bonham Carter: Acyanotic Congenital Heart-disease.
8 P.M. *Psychiatry* Dr W S Feldberg, F.R.S. Dr S L. Sherwood: Recent Experiments with Injections of Drugs into the Ventricular System of the Brain
SOUTH WEST LONDON MEDICAL SOCIETY
8 30 P.M. (Bolingbroke Hospital Wandsworth Common, S W 11) Mr Kenneth Walker Sexual Problems in General Practice
SOCIETY FOR THE STUDY OF ADDICTION
8 P.M (11 Chandos Street, W 1) Mr F T Hilliger Handwriting in Relation to Drug Addiction and Alcoholism.

Wednesday 20th

ROYAL SOCIETY OF MEDICINE
5 P.M *Comparative Medicine* Prof S P Bedson F.R.S., Dr Anthony Buxton, PH D., Mr G C Brander M.R.C.V.S Diseases of Pets Transmissible to Man
8 15 P.M *General Practice* Dr R. M S McConaghey: Collective Investigation
HYPNOTHERAPY GROUP
8 P.M (1 Wimpole Street W 1) Dr Denys Kelsey The Rationale of Hypno-analysis

Thursday 21st

ROYAL COLLEGE OF PHYSICIANS OF LONDON
5 P.M. Dr Cooke Aspects of Skeletal Disease (Second of two Lumleian lectures)
ROYAL COLLEGE OF SURGEONS OF ENGLAND
5 P.M. Mr N R. Barrett Primary Tumours of Rib. (Hunterian lecture)
MANCHESTER MEDICAL SOCIETY
7 P.M *Anæsthetics* (Joint meeting with Liverpool Society of Anæsthetists at Liverpool) Dr M. W Johnstone Mechanisms of Cardiac Arrest Dr George McLoughlin Hæmostasis

Friday, 22nd

ROYAL SOCIETY OF MEDICINE
8 15 P.M. *Obstetrics and Gynæcology* Dr A. J Wrigley Dr Derek Wylie Mr John Peel Hazards of Anæsthesia in Obstetrics
NORTH WESTERN TUBERCULOSIS SOCIETY
10 15 A.M (Joint meeting with British Tuberculosis Assn at Manchester University Manchester 13) Symposium Chronic Bronchitis

Notes and News

A BILL FOR EMERGENCY TRANSPORT

In April of last year a resident on Ailsa Craig needed urgent medical attention, so on two occasions the local lifeboat was hired to take him to a doctor on the coast Ayrshire Executive Council had met the expense (amounting to £16) out of the local mileage fund, on the grounds that if the patient had not come to the doctor, the doctor would have had to go to the patient, and an arrangement existed whereby the hire of the lifeboat, in such circumstances, was paid out of the mileage fund for Ayrshire The Department of Health for Scotland, however, confirmed the view of its auditors that there was no provision under the Act for paying the cost of transporting a patient to a general practitioner Since the patient had not attended a hospital, the sum could not be charged to the ambulance service

The department suggested that the patient should be asked to pay, but this request he ignored Accordingly, the department recommended that the local medical committee be asked to agree to the item being paid out of the mileage fund for Ayrshire The local medical committee, however, refused to accept this proposal, and the executive council has now, at the suggestion of the Department of Health, made application for the amount to be made a first charge on the mileage fund for Scotland

AN UNSATISFACTORY PATIENT?

The Northern Ireland General Health Services Board has been considering (says the *Belfast News Letter* of March 31) the request of a woman and her family that the board should assign them to a doctor's list The woman was removed from her doctor's list at his request, and she has so far been unsuccessful in finding another doctor in the district willing to accept her and her children as patients The children are in need of medical care and she ha[illegible]ingly turned to the board for help The board [illegible]pted the recommendation of its advisory medical committee that the patient should be asked to make a further attempt to find a doctor, and if this failed that the secretary of the local medical committee should be approached to see whether some arrangement could be made The difficulty appeared to be, the committee added, that the patients refused to carry out their doctor's instructions on treatment

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University of Cambridge

On March 19 the following degrees were conferred

M D—J R. Smythies
M Chir.—P F Boreham

University of Manchester

On May 11 the honorary degree of LL.D will be conferred on Sir Harry Platt, F.R C S

A diploma in psychological medicine has been granted to the following

H L English P A L Scott, B F Whitehead.

University of Dublin

At a recent examination for the diploma in gynæcology and obstetrics the following were successful

Saroj Kumar Chattopadhyay, Narendra Jagmohandas Choksey, lle J Gollan, Sister Mary Hyacinthe, Masuma Allah Jowaya n, E S Linton Shanti Malhotra Patrick O Shea, H B Perera M Rampersaud Arnold Rosin Bela Saha Ma Khin Aye Si Simon Mohamed El Kasimy Ahmed Tarshouby

ical Aspects of Traffic Accidents

onference on this subject is to be held at McGill University, real, on May 4 and 5 Prof Wilder Penfield, O M, F R.S, ive the introductory address Further particulars may ad from Dr Harold Elliott, Queen Mary Veterans ital, 4565, Queen Mary Road, Montreal

nating Need for Doctors

Evidence is now being invited by the committee set up by Minister of Health and the Secretary of State for Scotland, he chairmanship of Mr Henry Willink, to estimate the number of medical practitioners and the appropriate f medical students Invitations are being sent to organisations, but the committee is also willing to written evidence from other sources. Any person to submit views should send them ttee's secretary, Mr Phillip Muston, Row, London, W 1

Guy's Hospital

On Friday, May 6, at 5 P M, at the Medical School, London S E 1, Prof J Z Young, F R S, will give the Fison lecture on Memory Processes

West Midlands Physicians Association

The spring meeting of this association will be held at the Warneford Hospital, Leamington Spa, on Saturday, May 7, at 11 A M

Medical Society for the Care of the Elderly

The annual general meeting of this society will be held at the Whittington Hospital, London, N 19, on May 6 and 7

General Board of Control for Scotland

Mr D B Donald, a principal in the Department of Health for Scotland, has been appointed secretary to the board in succession to Mr J A MacGregor, who has retired after 45 years in the service of the board.

International Congress of Comparative Pathology

This conference will be held in Lausanne from May 26 to 31 under the presidency of Professor Fluckiger, director of the Federal Veterinary Office Further particulars may be had from the general secretariat, 19 rue César Roux, Lausanne

Institute of Diseases of the Chest, London

Dr J G Scadding is to give clinical demonstrations at the institute (in the grounds of the Brompton Hospital, Fulham Road, S W 3) on Fridays at 5 P M from April 22 to July 8 They are open to doctors without fee

Mental After Care Association

The annual general meeting of this association is to be held at 3 P M, on Friday April 22, at Westminster School, Little Dean's Yard, London, S W 1 Dr Henry Yellowlees and Sir Percy Barter will speak

Claire Wand Fund

The trustees of this fund invite essays on Postgraduate Education of Newly Qualified Doctors in Preparation for Entry into General Practice

The competition is open to any qualified doctor and the first prize is 200 guineas and the second prize 75 guineas The closing date is Jan 31, 1956 Further particulars may be had from the secretary of the fund, B.M.A House Tavistock Square London, W C.1

Royal Society

At a meeting of this society at Burlington House, London, W 1, on Thursday, May 12, at 4 30 P M, a film will be shown illustrating some of the research activities of the Istituto Superiore de Sanità in Rome Prof D Marotta, the director general, will give an introductory address, and Mr E M. Chain, F.R S, will speak on recent advances in carbohydrate metabolism

Premature Baby Unit

A small party was held at the Hammersmith Hospital on April 5 to welcome the 1000th baby to be admitted to the unit

The unit was opened on Dec. 1, 1947 Most of the babies cared for in the unit have been born in the obstetric department of the Hammersmith Hospital but over a third of admissions have been of babies born at home or in other hospitals and nursing homes. About 800 nurses from Great Britain and nineteen other countries have received periods of training

Human Relations in Industry

The Scientific Film Association is holding a conference on this subject from May 24 to 26 at Ashorne Hill, near Leamington Spa The four main sessions will be on films used as introduction to the job, films on human attitudes to work, films as a means of communication within industry, and films used for the training of management-worker relations Further particulars may be had from the general secretary of the association, 164, Shaftesbury Avenue, London, W C

Cushny Lectures

These lectures will be held at the Department of Pharmacology, University College, London, at 5 15 P M on Tuesdays and Fridays during May Dr S E Dicker will give the opening lecture on Renal Clearances in Mammalian Kidneys on Friday, April 29 The other speakers are Miss Gr Eggleton, D SC, Prof F R Winton, Dr Mary Pickford, Mr L E Bayliss, PH.D, Dr J D N Nabarro, Dr H. Harr Prof R A McCance, F.R S, Prof M L Rosenheim, and Prof G M Bull

TREATMENT OF TEMPORAL-LOBE EPILEPSY BY TEMPORAL LOBECTOMY

A SURVEY OF FINDINGS AND RESULTS

MURRAY A. FALCONER
M.Ch N.Z F.R.C.S
F.R.A.C.S
DIRECTOR,
GUY'S MAUDSLEY
NEUROSURGICAL UNIT

DENIS HILL
M.B Lond F.R.C.P., D.P.M
SENIOR LECTURER,
DEPARTMENT OF CLINICAL
NEUROPHYSIOLOGY
INSTITUTE OF PSYCHIATRY

ALFRED MEYER
M.D Bonn
PROFESSOR OF NEUROPATHOLOGY
INSTITUTE OF PSYCHIATRY

WILLIAM MITCHELL *
M.D Toronto D Psych.
RESEARCH ASSISTANT
MAUDSLEY HOSPITAL

DESMOND A. POND
M.D Camb M.R.C.P D.P.M.
SENIOR LECTURER, DEPARTMENT OF CLINICAL
NEUROPHYSIOLOGY INSTITUTE OF PSYCHIATRY

With the collaboration of R D HOARE M.B Lond. D.M.R
and G PAMPIGLIONE M.D Rome D Neuropsychiat.

EPILEPSY of temporal lobe origin is common and often disabling and may not be controlled by anticonvulsant drugs. Sometimes it is caused by a tumour angioma, or cyst, and it may cease when this is excised More often, however the underlying lesion is microscopic in size and hard to detect by clinical or radiological studies, or even when the brain is exposed at operation Indeed the clinical pattern of the seizures and their association with epileptic electro-encephalographic (E E G) discharges in one or both temporal lobes may be the only guides.

In the three years preceding March 1954 we treated 31 patients, with intractable epilepsy of this type by resection of the responsible temporal lobe and obtained cure or considerable relief of the epilepsy in 26 In all but 2 of these cases E.E.G had disclosed an epileptic focus confined to or predominantly in, one temporal lobe and the neurological and radiological investigations had not provided certain evidence of a space-occupying lesion Most of our patients had also exhibited a personality change or even a psychosis. As in the majority the epilepsy appears to have been improved, and in many the personality disturbances as well we feel that this method of treatment warrants a more extended trial.

Historical Background

It was Hughlings Jackson (1888) who first pointed out the association of the dreamy state" and the auras of psychical experience, of epigastric sensations, and of smell and taste hallucinations with lesions of the temporal lobe Since then attention has been directed to the type of seizure which may be ushered in by any of these auras, and which is neither petit mal † nor grand mal (although it may be associated with these) but is characterised by brief periods of dazedness with confused or semipurposive behaviour and by masticatory or sniffing movements.

This type of seizure which has been described variously as uncinate epilepsy psychomotor epilepsy psychical epilepsy and epilepsy with an intellectual aura, has come to be recognised as a common manifestation of temporal lobe epilepsy In its milder form however a temporal lobe seizure may consist merely in a sudden brief appearance of the sensory aura without dazing and in more severe attacks it may develop into a grand mal convulsion (Lennox 1951 Gastaut 1953 Falconer 1954) Further in possibly half the cases the victims of temporal lobe epilepsy develop an associated personality disorder or even a psychosis (Gibbs 1951, Mulder and Daly 1952, Hill 1953 Falconer 1953, Pampiglione 1953b), and in this respect temporal lobe epilepsy stands in striking contrast to focal epilepsy arising elsewhere in the brain The personality disturbance may take various forms, and often as the fits come under control with medication, the behavioural disorder increases The fits and personality disorder in patients under medical treatment thus often seem antithetic

An important advance in the recognition of this type of epilepsy resulted from E.E.G (Gibbs et al. 1948, Hill 1949, Jasper et al 1951 Gastaut 1953) Indeed foci of epileptic discharges can be demonstrated in one or both temporal lobes in from a quarter to a third of all patients with epilepsy This advance paved the way for the surgical treatment of otherwise intractable epilepsy by removal of the affected temporal lobe, especially when the E.E.G abnormality was confined to that lobe During the past four years several neurosurgical centres have reported their experiences of anterior temporal lobectomy in such circumstances and the published results have been encouraging especially as regards the control of the epilepsy but also as regards the amelioration of any associated personality disorder

Wilder Penfield in Canada is the chief pioneer in this field of surgery For many years his policy has been to submit patients with intractable epilepsy of various types to detailed neurological radiological, and E.E.G investigations, and to select for operation those in whom these preliminary investigations suggest a focal lesion (Penfield and Erickson 1941) Patients with pronounced psychological disturbances have been excluded (Penfield and Jasper 1954) The cranial operation has been performed under local anæsthesia to enable the surgeon to stimulate various parts of the cerebral cortex with electrical pulses while the patient is conscious, and so to ascertain from which regions of the brain the epileptic aura or even the epileptic fit can be provoked Penfield and Jasper (1954) have also taken electrical records from the exposed brain (electrocorticography) as an additional method of localisation.

Until very recently Penfield was loth to excise any part of the brain unless either an aura had been provoked from it, or there was some visible abnormality such as a scar an atrophic gyrus, or a small cyst Thus, Penfield and Flanigin (1950) reported that in 68 patients operated on between 1939 and 1949 macroscopic abnormalities had been observed in the great majority of cases: cortical excision had been carried out on E.E.G evidence in only 3 cases where there was no visible abnormality and in 7 cases no cortical excision had been done because no lesion was recognised and no aura or seizure provoked Although in 32 cases half or more of the temporal lobe was removed, the excisions generally did not include the deeper parts of the lobe such as the uncus, the amygdala, and the Ammon's horn (hippocampus). In the subgroup of 55 patients in which the epileptogenic focus was apparently identified success (i.e cure or only occasional seizures) was obtained in 29 and in a further 16 the frequency of seizures was lessened by at least half None of the patien who underwent craniotomy without excision was benefited and of the whole 68 patients only 1 died. Even after removal of the greater part of the temporal lobe Penfield and Flanigin found no alteration in behaviour no particular loss of memory no persisting aphasia and no defect in initiative or in capacity for decision.

Morris (1950) Bailey and Gibbs (1951) and Green et al (1951) all in the United States, were responsible for the nex advance—namely the removal of the affected temporal lobe o E.E.G evidence alone Unlike Penfield these workers include patients from mental hospitals, who had personality disorder as well as epilepsy Consequently they were forced to operat on their patients under general anæsthesia and were thereb precluded from studying the effects of stimulation in consciou patients as Penfield did. General anæsthesia in some patient proved advantageous, for it often increased the spike-di charges from the abnormal areas. Bailey and Gibbs (195 usually removed the greater part of the temporal lobe anteri to Labbé's (inferior anastomotic) vein, but spared the hip campal gyrus, the uncus the amygdala, and the Ammo horn. Morris (1950) performed a slightly less extensive op

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* In receipt of a grant from the Medical Research Council.

† This term is used here in the traditional sense of minimal seizures irrespective of the accompanying electro-encephalographic pattern.

6869

tion Green et al (1951), however, usually removed both the hippocampal gyrus and the uncus

More recently Bailey et al (1953) reported their collective experiences in 64 patients with both epilepsy and personality disorders In 33 of their patients the E.E.G abnormality was unilateral, and temporal lobectomy on this side abolished the seizures in 21 and much improved the psychological state in 15, enabling 14 to be rehabilitated In their remaining 31 cases spike discharging foci were observed in both temporal lobes, and after unilateral temporal lobectomy on the side of the dominant focus 7 patients were rendered free from seizures, and in only 3 was the psychiatric state sufficiently improved for the patients to be rehabilitated.

Workers at other neurosurgical centres have also reported their experiences, including Petit Dutaillis et al (1953) in France, Obrador (1953) in Spain, and our own group (Hill 1953, Falconer 1953, Pampiglione 1953b, Falconer et al 1953, Falconer 1954, Mitchell et al 1954)

The general experience has been that, as regards rehabilitation of patients, the surgery of temporal-lobe epilepsy compares favourably with the surgery of brain tumours or psychosurgery

Most of these neurosurgeons have performed these lobectomies by excising the superficial temporal gyri and then sucking out the deeper convolutions Usually the deepest parts of the temporal lobe, comprising the Ammon's horn, the amygdala, the uncus, and the hippocampal gyrus, have been left in situ Reports on the pathological changes present in the depths of the lobe have therefore been based on macroscopic impressions reinforced sometimes by fragmentary biopsies Penfield and his colleagues (Earle et al 1953, Penfield and Jasper 1954) emphasise the need to remove the uncus and the hippocampal gyrus in addition to the more superficial parts of the lobe, and describe cases which were not benefited by a superficial removal but were improved when these deeper structures were removed at a second operation

These workers also claim that the common pathological lesion underlying temporal-lobe epilepsy is "incisural sclerosis," which may involve most of the temporal lobe but affects particularly the uncus, the hippocampal gyrus, and the anterior part of the superior temporal gyrus They state that this condition was observed in 100 (66%) of 151 patients submitted to operation, but do not specify whether this sclerosis also extended to the Ammon's horn They hold that it is caused principally by birth trauma, and suggest that, during parturition, the mesial portions of one or both temporal lobes may become herniated through the tentorial opening as the result of head moulding, the anterior choroidal artery then becomes compressed against the free edge of the tentorium, causing local anoxia, and the sclerosis that follows this local anoxia develops in later life into an epileptogenic lesion

This is an attractive hypothesis, but from our own thological studies we believe that other processes also en involve the temporal lobes and thus give rise to epsy, birth trauma not being the exclusive cause of sclerosis Later events in childhood and adult life, as convulsions complicating childhood fevers, ular lesions complicating infections, the cyanosis iated with severe whooping cough, and head ies play at least an equal rôle (Meyer et al 1954) therapeutic results of surgery in Penfield's larger more recent series of cases have not yet been shed

Selection of Cases

e 30 patients ‡ whose relevant clinical features are ed in table I were referred from two sources 23 came from the epileptic practice of a psychiatric (Maudsley Hospital) and the remainder from a hospital (Guy's Hospital) Hence it is perhaps not prising that all but 1 of them also had a definite ality disorder The sexes were equally represented ages, at the time of operation, varied from 2½ to 56 years with 1 patient in the first decade of life, 5 in the second 9 in the third, 4 in the fourth 9 in the fifth, and 2 in sixth decade In 14 patients the epilepsy had b during the first decade of life, in 8 during the second decade, and in the remaining 8 patients at variable times between the ages of 20 and 50

The types of seizures conformed to the usual pattern of temporal lobe epilepsy, and some of the case histories have already been published (Falconer 1954, Falconer et al 1953, Mitchell et al 1954) Each patient exhibited a variety of attacks Amnesic seizures without a major convulsion but associated with auras of an epigastric, olfactory, gustatory, cephalic, or psychical character (psychomotor attacks) occurred in all Many patients had also noticed that these auras sometimes appeared without any dazedness or amnesia Grand mal (major convulsive) seizures, however, had occurred in 12 patients several times, in 9 they could be excluded, and in the remaining 9 they had either been very occasional or else the history was not sufficiently comprehensive to exclude them

The character and severity of the associated personality disturbances also varied considerably 10 patients exhibited psychopathic behaviour of the aggressive impulsive type with associated irritability and emotional lability Paranoid symptoms were observed in 9, and hysterical, anxiety, and depressive features in 7 A characteristic feature was a long history of emotional disorder and of poor adaptation to social demands, work, and sexual life Psychotic episodes in association with fits, necessitating admission to observation wards or mental hospitals, had occurred in 7 2 patients had been confined in mental hospitals as certified patients for more than a year, and 3 had been in remand homes or before the courts because of antisocial behaviour

Most patients had been under medical supervision for many years, and their attacks had continued in spite of long and adequate trials of various anticonvulsants Exceptions, however, were 3 cases (nos 9, 20, and 30 in which the suspicion of tumour was aroused because the seizures had appeared only recently in an adult patient, because the temporal horn was slightly distorted in the pneumo encephalograms, or because the E.E.G showed irregular slow-wave activity in the temporal region In several other patients the preoperative radiological investigations indicated either a definite space-occupying lesion—e g, a tumour, and an angioma—or porencephaly, but, as the operation on these patients was limited to local excision of the lesion, they have been excluded from this present study The various patients which we have included in table I have now all been followed up for periods of one to four years

Methods of Study

Before operation, all our patients, besides having a comprehensive psychiatric assessment, were submitted to detailed neurological, electro encephalographic, and neuroradiological examinations These inquiries were always supplemented by interrogation of the relations as well as by summaries of the notes from other hospitals Many patients also underwent detailed psychometric tests

Neurological Findings

In most patients neither the neurological examination nor the analysis of the cerebrospinal fluid showed any significant abnormality There were, however, 3 exceptions Two patients (cases 7 and 18), both of whom had sustained severe closed head injuries, exhibited various residual cranial-nerve palsies, and an adolescent patient ase 17) presented an infantile hemiplegia which had ppeared at the age of 3 years as a complication of easles.

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‡ unately the second patient on whom we operated died ly after operation our only fatality to date Although ioned in earlier communications (Hill 1953 Falconer 1953 iglione 1953b Meyer et al 1954) she has been excluded his review because there was no opportunity of observing [illegible] ave followed the operation had she

E G Findings

Each patient had been repeatedly examined, often ver many years with scalp electrodes placed in various ombinations over the convexity of the skull Generally uch routine studies disclosed spike or sharp wave dis harges around the sylvian inferior frontal or anterior r mid temporal regions Occasionally however such outine studies were indeterminate In all cases we found hat special E.E.G techniques were necessary before the bnormality could be clearly and properly located (Hill 1953 1955 Pampiglione 1953b) These techniques include the placing of needle electrodes beneath the *temporal lobes (sphenoidal electrodes), and a midline* basal lead (chin nasopharyngeal or nasal) in addition to the usual scalp leads over the convexity as well as the use of induced narcosis (resulting from either quinalbarbitone by mouth or thiopentone intravenously) for often the epileptic discharges become activated as the patient passes into sleep

In 28 of our 30 patients a definite spike or sharp wave discharging focus was demonstrated in the temporal regions (table I) In 19 patients the focus was confined to one side generally being apparently closer to the sphenoidal lead than to the leads over the temporal convexity

TABLE I—CLINICAL MATERIAL AND RESULTS OF OPERATION

			Clinical features						Pathological features			Postoperative Results			
Case no.	Sex	Age (year)	Age at onset of epilepsy (years)	Family history of epilepsy	Other possible causal factors	Grand mal in addition to psychomotor seizures	Personality disorder (P = psychosis)	Temporal-lobe E.E.G focus	Side of operation	Small macroscopic focal lesions	Sclerosis of Ammon's horn	Fits	Personality	E.E.G	Working ability (preoperative to postoperative)
1	F	5½	1½			–	++	Unilateral	L	Hemangioma calcificans		Free	Improved	Slightly improved	Infant→at school
3	M	25	18		Difficult birth and pugilism	++	++	Bilateral	R & L		–	Occasional—died 6 *months* after second lobectomy of grand mal status	Worse	Not better	Some→ none
4	M	32	2			++	++	Unilateral	L		Not available	Free	Improved	Slightly improved	None→ full
5	F	15	6			?	++	Unilateral	L	Hemangioma calcificans		Free	Improved	Improved	None→ full
6	M	45	2			–	++ (P)	Unilateral	R		+	Occasional	Not benefited	Not better	Some→ slight improvement
7	M	45	18	Yes	Severe head injury	++	++ (P)	Bilateral	R		–	Less	Worse	Worse	None—unchanged
8	M	22	2	Yes	Difficult birth	++	++	Bilateral	R		++	? Fit-free for 2 years—then died from grand-mal status	Not benefited	Worse	None—unchanged
9	M	23	21		Mild head injury	–	–	Unilateral	L	Meningioma		Free		Improved	Some→ full
10	M	40	30		Chorea in childhood	Occasional	+	Bilateral	L		Not available	Occasional	Improved	Improved	Some→ full
11	F	43	31			Occasional	++	Bilateral	L	Capillary angioma		Occasional	Not benefited	Improved	Some—unchanged
12	M	23	8			–	++ (P)	Unilateral	L		–	Free	Improved	Improved	Full—unchanged
13	M	13	3		Difficult birth	?	++	Unilateral	L		++	Free	Improved	Improved	None→full
14	F	21	2		Precipitate birth	++	++	Unilateral	L		–	Less	Slightly improved	Slightly improved	None—unchanged
15	F	25	11		Difficult birth	++	++	Bilateral	L		++	Free	Not benefited	Improved	None—unchanged
16	M	23	2	Yes	Teething convulsions	Occasional	+	Unilateral	R		++	Occasional	Improved	Improved	Some→ full
17	F	12	4		Hemiplegia complicating measles	++	++	Unilateral	L		++	Free	Improved	Improved	No school→school
18	[illegible]	47	30		Severe head injury	++	++ (P)	Unilateral	R	Cicatrix		Occasional	Not benefited	Slightly improved	None—unchanged
19	F	40	18			?	++ (P)	Bilateral	L	Angioma		Occasional	Improved	Slightly improved	Some→ full
20	F	48	47			Occasional	+	No focus	L	Small infarct secondary to arterio-sclerosis		Occasional	Improved	Worse	Some→ full
21	F	22	2		Whooping cough 1 month before onset	Occasional (only at onset)	++ (P)	Unilateral	L		++	Free	Improved	Slightly improved	None→ full
22	F	16	9	Yes		–	++	Unilateral	R		++	Free	Improved	Improved	None→ full
23	M	36	2			++	++	Unilateral	R		++	Occasional	Slightly improved	Improved	Full—unchanged
24	F	23	1		Difficult birth	–	++	Bilateral	L		++	Occasional	Improved	Improved	None→ some
25	F	30	14	Yes	Precipitate birth	++	+	Bilateral	L		+	Occasional	Not benefited	Slightly improved	None→ some
26	M	32	17	Yes	? Otitis media	++	+	Unilateral	L		–	Occasional	Improved	Improved	Full—unchanged
27	F	45	3		Precipitate birth and otitis media	?	++	Unilateral (Theta focus only)	L		–	Free	Improved	Not better	None→ some
28	M	56	50		Malignant malaria	–	++	Unilateral	R	Oligodendro-glioma		Occasional	Improved	Slightly improved	None→ some
29	M	[illegible]	39		Chronic alcoholism	++	++ (P)	Unilateral	L		–	Occasional	Not benefited	Improved	None→ some
30	F	51	40			?	+	Unilateral	R	Oligodendro-glioma		Free	Improved	Slightly improved	Some→ full
31	F	[illegible]	1		Scarlatina, whooping cough, and otitis	–	+	Unilateral	R		+	Occasional	Slightly improved	Improved	Some→ full

The frequency of these discharges varied from only a few times in each record of half an hour's duration to a firing rate of more than 100 times a minute Sometimes *subsidiary discharges were also evident in the suprasylvian regions* In 9 *patients spike discharges were* evident in both temporal lobes, but there was a predominance on one side, and this side was selected for operation Cases in which equally active and independent discharging foci were present on the two sides were rejected for operation In the remaining 2 patients a focus of 5–6 cycles per sec was present in 1 (case 27), while no epileptic activity was observed in the other (case 20), even on several occasions In case 20, however, the fits were of recent onset, and pneumo encephalograms showed that, although there was no localised distortion of the ventricles, the septum lucidum was shifted 2 mm to the opposite side A tumour was suspected, but at operation no tumour was seen Temporal lobectomy was performed because the anterior temporal region looked pinker than normal and electrocorticography showed diminished electrical activity there The patient was subsequently relieved of seizures, and pathological examination disclosed a small infarct

Radiological Findings

Straight radiographs of the skull were usually normal, but in a quarter of the cases one half of the cranial cavity was slightly smaller than the other, owing particularly to smallness of the middle cranial fossa, and indicating a defect of development dating back to early childhood In cases 1 and 19 patchy calcification was visible near a vascular lesion Carotid arteriography was performed in a few patients, usually with normal findings, even in 2 with angioma Pneumo encephalography, however, proved more helpful, and was done in all the patients, care being taken to outline the temporal horns of the lateral ventricles Although cases with definite distortion of the ventricular outlines, indicating a space occupying lesion of an appreciable size, were excluded from our series, *close scrutiny of the films showed slight asymmetry* in a high proportion of cases Thus pneumo-encephalographic evidence of either a slight smallness of one cerebral hemisphere or a focal dilatation of one temporal horn was seen in half the cases Almost always these radiological signs were on the same side as the E E G focus, but in 4 cases (nos 5, 18, 28, and 30) they seemed to be divergent, the temporal horn on the side of the E E G focus appearing smaller In all 4 cases we operated on the side of the electrical abnormality, and our action proved correct, for in each case a small macro-copic lesion was found (hæmangioma calcificans 1, icatrix 1, oligodendroglioma 2), and subsequently the itients were relieved of epilepsy When, therefore, the entricular outlines are asymmetrical, and one wonders whether one side is slightly dilated or the other side ightly narrowed, the pneumo encephalographic appearances should be interpreted in the light of the electro-ncephalographic findings If the ventricle on the same ide as the focus is small, a tumour may be present

Conduct of Operation

rom the work of Penfield (Penfield and Erickson 1941, field and Rasmussen 1953) as well as from our own erience of tumour surgery, we knew that the temporal anterior to Labbé's (inferior anastomotic) vein can erally be removed, even on the dominant side, without ucing permanent aphasia At the outset we therefore pted the policy of removing in one piece as much of ffected temporal lobe as possible without harming the t In this way we hoped not only to eradicate the ogenic lesion but also to secure the tissue in a itable for detailed histological examination

a

ion is usually done under local analgesia but, if the patient is very apprehensive or difficult to control, general anæsthesia is used. (Endotracheal nitrous oxide, oxygen, and trichloroethylene constitute a useful *non-explosive* anæsthetic which disturbs the E.E G patterns but little and allows electrical equipment to be used without risk of an explosion.) An intravenous saline drip *is set up so that during* electrocorticography an intravenous injection of thiopentone (0 10–0 15 g) can be given via the drip for its potentiating effects Also, if the operation has been started under local analgesia, its later *painful stages* can readily be completed under intravenous anæsthesia The pain incidental to the later stages of removal of the temporal lobe can also be lessened by injecting the gasserian ganglion with a *local* analgesic solution (Penfield and Baldwin 1952)

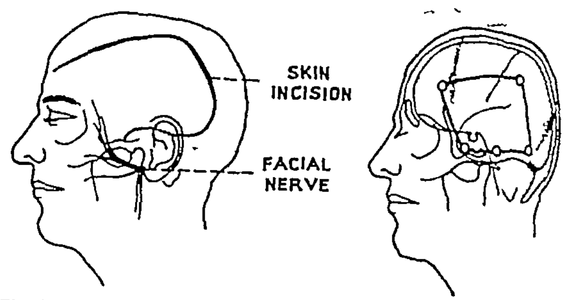


Fig 1—Siting of scalp and bone flaps for anterior temporal lobectomy

Incision and Bone Flap

The positions of the scalp incision and of the bone flap are shown in fig 1 The use of this particular incision avoids damage to the uppermost branches of the facial nerve, and the bone flap pedicled on the temporal muscle affords a maximum exposure of the temporal lobe and of the adjacent portions of the frontal and parietal lobes Occasionally an unsuspected lesion, such as a tumour or an angioma, will then present, in which *case it should be excised Usually, however, the surface* of the brain looks normal, although fairly often the temporal lobe looks small

Electrocorticography

This is not essential if the preoperative E.E G studies have been adequate , for an anterior temporal lobectomy can be confidently done on their evidence alone It is, however, very helpful in confirming the site of the focus and the presence of any abnormal cerebral tissue

Flexible electrodes (insulated except for their tips) are placed underneath the temporal and frontal lobes and at the temporal pole, and several standard electrodes are placed over the surface of the exposed brain A common finding is of spike discharges located at the pole, at the convexity close to the pole, or in the anterior part of the hippocampal gyrus In some cases spike discharges may also be observed outside the projected area of the excision—e g , in the posterior temporal and suprasylvian regions The significance of such discharges is not known, but our experience so far *indicates that, provided the main focal abnormality lies within* the part of the lobe which is to be excised, relief or improvement of the epilepsy can subsequently be expected. A most useful finding is that of areas where fast rhythm activity is not induced when intravenous thiopentone 0 10–0 15 g is given Such areas are found fairly often in the anterior temporal region and suggest the presence of diseased cerebral tissue in the vicinity (Pampiglione 1953a) Indeed it is our impression that such areas, if present, give a better clue to the location of the underlying pathological lesion than do *areas of frequent spike-discharges*

Stimulation Tests

In patients operated on under local analgesia we have then stimulated various parts of the temporal lobe with a pulsating electric current, as does Penfield In several instances we have provoked hallucinatory phenomena from the temporal lobe, but not consistently We have found, however, that local epileptic discharges, which are sometimes associated with ictal phenomena, can be induced from various parts of the cortex both in and remote from the temporal lobe, as well as from the region of the Ammon's horn (hippocampus) and the amygdala. The induced seizures sometimes resemble the patient's spontaneous seizures or they may differ. The induction of an aura or a brief seizure therefore from a point on the cortex, should not be taken as evidence that that point was the site of the epileptogenic lesion unless the induced attack is identical with the spontaneous seizures.

Technique of Operation

The steps of our operative excision are outlined in fig 2. The extent of this resection is similar to that practised by Penfield (Penfield and Baldwin 1952), but instead of removing the deeper parts of the temporal lobe by suction we try to excise the lobe in one piece. We also now spare more of the superior temporal convolution than we did originally (Falconer 1953), both to obviate aphasia and because this gyrus usually seems free from pathological change.

Starting at the sylvian point the incision runs obliquely to the inferior border of the lobe just in front of Labbé's (inferior anastomotic) vein a distance of usually 6–7 cm. from the pole. It is then deepened to uncover the lower and anterior portion of the insula (island of Reil). The section of white matter is made with a fine bore metal sucker (2–3 mm in diameter) hæmostasis being secured by finely controlled diathermy. The surface of the insula is protected by leaving in situ the pia mater investing the temporal operculum. Next the white matter between the lower border of the insula and the roof of the temporal horn is divided thus laying open the temporal horn with the Ammon's horn in its floor and the choroid plexus above this. The removal of the lobe is then completed by continuing the incision across the hinder end of the Ammon's horn on to its medial border and by dividing the most medial portion of the uncus and the fimbria hippocampi. During this last stage care is taken to keep inside the pial covering of the uncus and the hippocampal region to avoid damage to the third cranial nerve the posterior cerebr artery and the mid brain. An attempt is made to include i the specimen much of the amygdalar complex which lies abov and medial to the tip of the temporal horn. In closing th craniotomy the dural incisions are sutured to prevent bloo from the bone and scalp flaps from seeping into the ventricul system.

Incidental Effects of Operation

Immediate Postoperative Effects

We had 1 death among more than 40 patients, an Penfield and Flanigin (1950) had 1 in 68. Although th postoperative convalescence has generally been smoot a few focal motor seizures, usually involving the fac have been observed in about a third of our patients a some time during the first ten days following operatio Penfield and Jasper (1954) report similar observation These seizures are presumably due to reactionary œdem in the brain bordering on the area of excision, and the occurrence does not indicate that the patient's pre operative seizure will persist or return. Again in mos patients after removal of the greater part of the le temporal lobe, transient aphasia occurs which disappear in a week or ten days. Transient diplopia, and occasionall even ptosis, both due presumably to traction on th third nerve during the elevation of the temporal lobe have been seen in a few patients but have alway disappeared.

Permanent Neurological Effects

Most patients exhibit a partial homonymous hemi anopia generally limited to the upper quadrants. Penfield (1954) states that, if the excision is limited to less than 6 cm from the temporal lobe no defect of the visual field results. If however 6 cm or more is removed, an upper quadrantic homonymous hemianopia results and if more than 8 cm is removed a complete homony mous hemianopia follows. Our own experience shows a much greater variation than this because 1 patient even after a 6-cm. excision showed a nearly complete homonymous hemianopia while others after an 8-cm excision showed scarcely any loss.

As regards speech, in a third of patients in whom the dominant temporal lobe has been removed there was a slight but permanent nominal aphasia. The [illegible] of the difficulty was usually apparent in naming [illegible] one of ten common objects. 2 patients have noticed their speech difficulty themselves but [illegible] has been appreciably [illegible] by them. Penfield [illegible] (1954) report [illegible] persistent aphasia [illegible] temporal lobe [illegible] part of the [illegible]

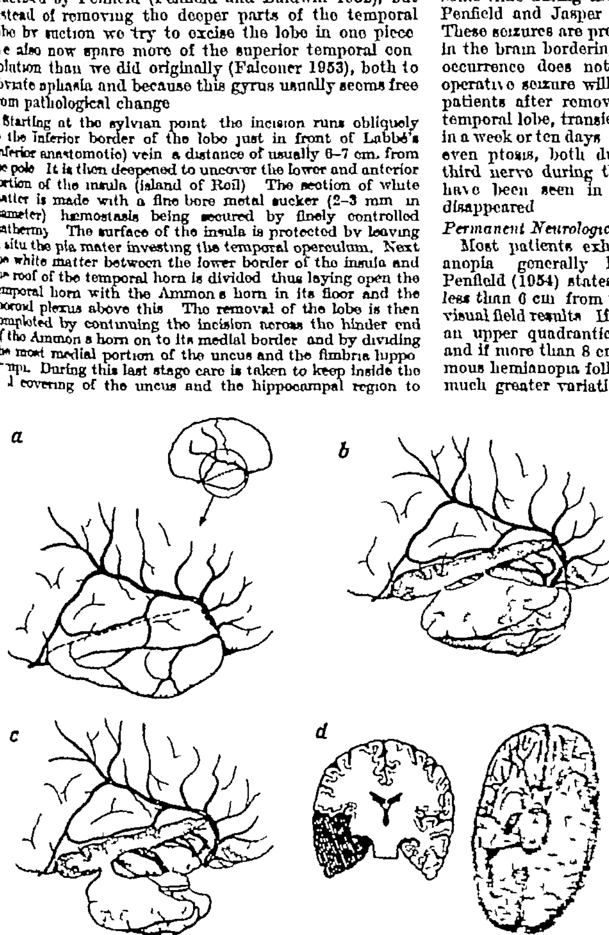


Fig. 2—Stages of temporal lobectomy: a, first stage showing the line of incision in relation to sylvian vessels and Labbé's vein; b, second stage, showing insula uncovered and temporal horn entered posteriorly; c, third stage showing temporal horn opened along its roof, Ammon's horn in its floor with choroidal plexus lying above it; d, representation of extent of removal of temporal lobe on completion of operation.

(Modified from *Proceedings of the Royal Society of Medicine* [illegible])

TABLE II—OVER ALL RESULTS OF OPERATION

As regards epilepsy (30 patients)			
Fit-free	12	Marked improvement	26
Occasional seizures only	14		
Still continuing fits, but frequency less		Slight benefit only	2
Improvement in epilepsy but not in personality or working ability (died later of grand mal status)			2
As regards personality disorder (29 patients)			
Much improvement	17	Definite benefit	20
Slight improvement	3		
No benefit or worse			9*
As regards working ability (30 patients)			
Regained full ability (including schooling)	14	Working	24
Partial improvement (no working ability to some)	5		
Previous ability to work unchanged (Full ability 3 some 2)	5		
Still no working ability			6*

* Includes the 2 patients who subsequently died of status epilepticus

(1955), however, have observed that, after removal of the dominant temporal lobe, there is usually a slight impairment in the patient's ability to learn new verbal material This difficulty is not present after removal of the non dominant temporal lobe It occurs even in the absence of aphasia Only 2 patients, however, have noticed it themselves one was a furniture packer (case 4) who found himself slow to learn new techniques of packing, and the other was a business man (case 9) who found it hard to describe his way through the streets of London, although he himself could find his own way, either on foot or by motor-car, without difficulty No difficulty exists in learning new material which is presented visually rather than auditorially

Therapeutic Effects of Operation

General

The salient data for our various patients are set out in table I, the follow up period varying from one to four years In assessing the results we have discounted any fits or behavioural disturbances observed during the early postoperative period Many patients have continued to take anticonvulsants, usually in smaller amounts than before, because our general policy has been to wait for two or more years' complete freedom from seizures before ceasing such medication altogether Several patients, however, ceased taking drugs on their own initiative, and a few did this without untoward effect, although 5 others exhibited an occasional fit (table III) One must remember, of course, that before operation all the patients had continued having fits in spite of regular and adequate medication

The over all results are summarised in table II They show that 26 patients were much benefited as regards their epilepsy, and 20 of the 29 who had a personality disorder were correspondingly improved Thus, whereas some improvement in the epilepsy was often observed, improvement in personality was less certain, and a third of the patients derived no benefit in this respect 12 patients are now fit-free, and 14 others have had occasional seizures The nature of these occasional seizures is summarised in table III, where it will be seen how frequently their appearance was related to the cessation of drugs, which were then generally reinstituted Of the 2 patients whose seizures were only slightly reduced case 7 showed radiological evidence of bilateral cortical atrophy following a severe head injury, and case 14 had a recrudescence of seizures during a pregnancy

As regards the postoperative psychological changes, in more than half our patients the improvement was striking, even in 3 of the 7 who had a psychosis Some patients whose epilepsy and concomitant mental difficulties have plagued them most of their lives need social measures or superficial psychotherapy to assist their timorous steps to establish themselves in a new and fit-free li [illegible] in all non analytic psychotherapy, precautions must be taken against a state of morbid dependency developing which will prevent rehabilitation of the patient In 5 patients (cases 7, 15, 23, 26, and 31) electroconvulsion therapy has been given for postoperative depressive states, and in 3 has been efficacious

Clinical improvement was often associated with improvements in the E.E G and in working capacity This last, however, more closely paralleled the changes in personality than the changes in the epilepsy Thus before operation only 3 patients had full working ability, and 15 had almost none After operation 24 are working and 17 have full working ability The 6 patients who are still not working are all handicapped by their persistent personality disorder rather than by epilepsy

In view of the often cited observations of Klüver and Bucy (1939) on the indiscriminate hypersexual behaviour shown by monkeys after bilateral temporal lobectomy, some observations on the sexual attitudes of our own patients may be pertinent

The necessary information could be obtained in 15 of our patients, and two clear patterns could be discerned those who did very well both in the epileptic and mental spheres showed an increase of sexuality by either intercourse or masturbation, and those who did poorly were impotent to various degrees Case 12 with fetishism (Mitchell et al 1954) and case 13 (Pond and Bidwell 1954) with sexual perversion were relieved of these disabilities Another patient (case 5) who masturbated openly several times a day and made homosexual advances during the second postoperative month, showed no improvement in his preoperative personality Our 1 patient with bilateral temporal lobectomy (case 3) has shown no sexual interest

TABLE III—ANALYSIS OF PATIENTS WITH OCCASIONAL FITS AFTER OPERATION

Case no	Follow up (years)	Particulars of fits
6	3½	Averages 4 amnesic seizures a year
10	2	2 amnesic seizures during first year
11	2	1 amnesic seizure recently on stopping drugs
16	1¾	2 minor focal motor seizures
18	1½	4 amnesic seizures on day of father's death
19	1½	1 amnesic seizure when drugs stopped abruptly
20	1½	5 amnesic seizures plus occasional olfactory hallucinations
23	1¼	Possibly 5–6 convulsive seizures but has not taken drugs
24	1¼	1 amnesic seizure at time of emotional stress
25	1	1 amnesic seizure recently plus occasional illusory sensations
26	1	1 amnesic seizure when off drugs plus auditory hallucinations on 3 occasions
28	1	Possibly 10 amnesic seizures, a reduction of more than 75%
29	1	1 amnesic seizure plus occasional dizzy sensations
31	1	1 focal motor seizure on stopping drugs

So far our experience of bilateral temporal lobectomy has been limited to 1 patient, who was not improved as regards personality, although after lobectomy on the second side he seemed relieved of his epilepsy Our patient exhibited a profound disturbance of memory but no aphasia He died, six months later, of status epilepticus Few details of similar cases have been published Scoville and his associates (Scoville 1954 Scoville et al 1953) report that after resection of the mesial portions of both temporal lobes in patients with mental illnesses but without epilepsy there is usually no great physiological or behavioural disturbance, although 1 of their patients suffered a grave loss of memory Bailey et al (1953) report having performed a two stage bilateral temporal lobectomy in 4 patients, of whom 2 were improved slightly and 2 were unchanged No-one has yet reported a case which was much benefited by bilateral temporal lobectomy

One other patient in our series (case 8) died of a grand mal status epilepticus twenty-five months after operation Until that time he had described himself as seizure free He had, however, a psychopathic personality which had not been improved, as well as a discharging focus in e opposite temporal lobe. Furthermore, towards the d of the first year he had presented a localised disten on of the operative cavity due to the development of a embrane across the cut end of the temporal horn with ontinued secretion of cerebrospinal fluid by the choroid lexus which had been left in situ. This distension had d to hemiparesis. The mechanism strongly suggested he local hydrocephalus of the temporal horn described y Cairns et al. (1947) as occasionally following gunshot ounds involving the trigone of one lateral ventricle. This complication so far has only occurred once in our experience, and it was treated by diathermy coagulation of the offending portion of the choroid plexus and was followed by an apparently successful recovery from the hemiparesis.

Correlation between Preoperative and Therapeutic Results

When the preoperative data were analysed in the light of these postoperative results, interesting correlations appeared (table IV). Such factors as age, sex, duration of symptoms, and whether the focus was on the right or left side were without obvious influence; but the presence of a second although subsidiary discharging focus on the opposite side and the occurrence of grand mal seizures (even only a few each year) definitely influenced the results for the worse. Repeated sphenoidal E.E.G. investigations under narcosis spaced over several weeks are necessary to exclude a contralateral focus. The best results were obtained in 13 cases in which the epileptic discharges were strictly confined to one temporal lobe and there had been only an occasional grand mal seizure or none. Every such patient was much benefited as regards his epilepsy and all but 1 as regards his personality also. This exception (case 6) is a man aged 45 with a history of psychomotor attacks and a paranoid personality disturbance dating back to early childhood. He has never had a satisfactory personality, and although employable he is still paranoid. It might be argued that, had this man been operated on while still in his teens or even earlier, the end result might have been better. To restore a normal personality to a patient who has not had one since early childhood might seem impossible; but this was accomplished in at least 2 patients (cases 13 and 21) who were operated on at the ages of 13 and 22.

A history of an occasional or uncertain attack of grand mal had little influence, for the results were no different from those obtained in cases in which grand mal could be excluded. The occurrence of separate bilateral discharging E.E.G. foci or of more frequent grand mal seizures (even only one or two each year) worsened the results slightly. But our worst results were when these two factors were combined, for in the 5 cases in which this conjunction occurred only 2 patients were benefited as regards epilepsy, and none as regards personality.

BLE IV—CORRELATIONS BETWEEN PREOPERATIVE DATA AND RESULTS OF OPERATION

Data	No of cases	Epilepsy		Personality disorder	
		Marked improvement	Little improvement	Definite benefit	No benefit
e of electro-encephalographic focus					
Unilateral	20	19	1	15	4
Bilateral	9	6	3†	3	6†
currence of grand mal					
No grand mal	8	8	0	6	1
Very occasional or uncertain grand mal	10	10	0	9	1
Grand mal	12	8	1†	3	†
ccurrence of electro-encephalographic focus with grand mal					
Unilateral focus with no, occasional or uncertain grand mal	13	13	0	11	1
Unilateral focus with grand mal	7	6	1	5	2
Bilateral focus with no, occasional or uncertain grand mal	4	4	0	3	1
Bilateral focus with grand mal	5	2	3†	0	5†

One patient had no personality disturbance either preoperatively or postoperatively.

Includes 2 patients who after apparent improvement died from grand mal status epilepticus.

Pathological Findings

In every case some pathological change of varying nature and degree was found in the resected temporal lobe. A preliminary report on this subject has only recently appeared (Meyer et al. 1954) and we shall therefore offer only a few generalisations. The pathological lesion has usually been microscopic rather than macroscopic; but the variety of lesions observed has been wide, in keeping with the long-established dictum that epilepsy depends more on the situation of a lesion than on its precise pathological nature, and that epilepsy can result from different processes.

In 9 cases a small macroscopic lesion was found (cerebral tumour 3, hæmangioma calcificans 2, angioma 2, infarct 1, cicatrix 1). The 2 cases of hæmangioma calcificans (cases 1 and 5) have already been reported (Falconer et al. 1953). These 9 cases, as might be expected since the whole lesion was excised, were all greatly benefited as regards epilepsy; but in 2 there was no corresponding improvement in personality. In 1 of these patients (case 18) there was radiological evidence of a widespread post-traumatic cerebral atrophy in addition to the localised cicatrix. In the other (case 11) a tiny capillary angioma was found in the uncal region, and this patient has continued to have a paranoid personality which has now lasted ten years. In this case, as in the other case of angioma (case 19), a second but subsidiary E.E.G. focus in the opposite temporal lobe disappeared after operation. Presumably the presence of such a focus in the opposite temporal lobe cannot be regarded as evidence of pathological change in that temporal lobe. In only 4 cases had we suspected from preoperative investigations that there might be a space-occupying lesion. In 2 of these (cases 9 and 30) pneumo-encephalography suggested slight indentation of the temporal horn; in the 3rd (case 1) an area of calcification was visible in the radiographs but without indentation of the temporal horn; and in the 4th (case 10) a calcified angioma had been removed from the superficial part of the temporal lobe at another neurosurgical unit, but the fits had continued without abatement. It was only after the deeper parts of the temporal lobe, including the uncus and the Ammon's horn, had been removed that her fits ceased and her personality was much improved.

In the remaining 21 cases the lesions were microscopic and less circumscribed. The complexity of these changes has been previously emphasised (Meyer et al. 1954) and the present analysis is no more clarifying. In all the cases the non-specific changes of meningeal fibrosis, focal or diffuse cortical atrophy, marginal gliosis, and gliosis of the white matter were present in various proportions. In 6 cases (cases 3, 7, 12, 14, 26, and 27) such lesions were the only ones observed, and the intensity of the changes was often comparatively slight. Degenerative arterial changes were prominent in case 29. In 12 of the 21 cases, however, sclerosis of the Ammon's horn was a conspicuous feature. In our more recent material we are learning that sclerosis and other changes may also be present in the amygdalar region. Pathological changes in this latter region have not hitherto been reported; but sclerosis of the Ammon's horn has been described by many observers during the past seventy years as occurring with this same degree in the brains of chronic epileptics who come to necropsy. The case material for most such studies, however, has usually been provided from institutions for chronic mental patients and so may well have contained a very high proportion of temporal-lobe epilepsy (Sano and Malamud 1953)

The ætiology of the various lesions in this subgroup of 21 cases with "microscopic" changes is obscure 6 patients had a known family history of epilepsy, and this proportion agrees with most published statistics regarding "idiopathic" epilepsy (Wilson 1940) It probably indicates a hereditary predisposition leading to lowering of the neuronal thresholds for epileptic activity rather than the actual inheritance of structural lesions Difficult birth was noted in 5 patients (a proportion which is undoubtedly of statistical significance) and precipitate birth was recorded in 3 other patients According to Penfield's hypothesis (Earle et al 1953, Penfield 1954) sclerosis of the Ammon's horn is due principally to birth trauma, whereas according to the classical view of Spielmeyer (1930) it is provoked by anoxia of the brain during the cyanotic stages of grand-mal seizures In our material, however, only 4 of our 12 patients with sclerosis of the Ammon's horn had had a pathological birth, and in 6 others the birth was reported as definitely normal In 7 cases grand-mal seizures had been observed, but in 4 they could be excluded A possible alternative cause in 4 patients had been a period of coma, cyanosis, or convulsions associated with an acute febrile illness in early childhood In 3 patients with sclerosis of the Ammon's horn no obvious cause was forthcoming Encephalitis did not appear to be a factor

Thus the pathological findings in our cases indicate that there is no one preponderant lesion in temporal-lobe epilepsy, but that the clinical picture can be provoked by different lesions due to differing causes

Illustrative Case-report

The case histories of several patients have already been reported (Falconer et al 1953, cases 1 and 5, Falconer 1954, cases 8, 13, and 20, Mitchell et al 1954, case 12, Pond and Bidwell 1954, case 13) The following case, not previously published, illustrates a striking recovery in both epilepsy and personality

Temporal lobe epilepsy, associated with a paranoid hallucinatory psychosis, relieved by anterior temporal lobectomy Pathological lesion sclerosis of Ammon's horn

Case 21—A woman, aged 22, referred by Dr L C Cook and Dr D M Lieberman, had had her first fit, a grand mal status epilepticus at the age of 19 months, a month after an apparently uncomplicated attack of whooping cough Her birth had been normal, and family history clear of epilepsy Shortly afterwards she started having frequent attacks of a psychomotor type without convulsions

The attacks usually began with an epigastric sensation, and in later childhood with also a vision of a "silvery man in armour" They would last from a few seconds to a few minutes, and during them she would appear frightened, wring her hands, and make swallowing movements In the longer attacks she became violent Various drugs had been tried but did not control the attacks, and between the ages of 7 and 12 years she was cared for in an epileptic colony From early life her personality had been abnormal she was liable to frequent temper tantrums and delinquency, and at times to sexual exhibitionism At puberty she had a schizoid personality, and this and her epilepsy rendered her unemployable During the past two years she had developed a paranoid hallucinatory psychosis She sat withdrawn and solitary, alternately smiling and grimacing, punctuating this with anxious glances, and listening to imaginary voices She said that people were controlling all her actions with wireless in the floor and roof, that people were always looking at her because she was a whore, and that other people were accusing her of stealing money She had attempted suicide and recently had been certified

On admission neurological examination was negative Repeated E E G examinations had always revealed a spike discharg[illegible]s in the left anterior temporal region, most clearly [illegible] the convexity but also evident at the sphenoidal lead Radiography of the skull and pneumo-encephalograms were normal

At operation the left temporal lobe appeared small, and electrocorticography confirmed the presence of spike discharges in the anterior temporal region The anterior 6 cm of the lobe was resected, gross sclerosis of the Ammon's horn being subsequently confirmed histologically, together with fairly heavy marginal gliosis and moderate gliosis of the white matter throughout the specimen.

Postoperatively the patient made a dramatic recovery She had two minor "blank" spells, coinciding with the first and second menstrual periods following operation, but subsequently she became seizure free She gradually lost all her hallucinations and became friendly and active in her home. Three months after operation she became a shop assistant, and seven months later she changed her occupation to that of agricultural worker Thirteen months after operation, when she reported back to hospital for review, she appeared shy but mentally normal, neat and careful of her appearance. She had given up her tablets several months previously Her work reports were good She had gained a stone in weight and looked robust and healthy Her menses, which previously had always been scanty and irregular, were now regular and normal Her only neurological sign was a right upper quadrantic homonymous hemianopia, which had persisted since operation The E.E G findings were considerably improved, focal spike discharges being no longer evident The patient and her family were delighted with her recovery

Discussion

The high frequency with which pathological changes have been found in the resected temporal lobes, and the high rate with which relief or improvement, particularly of epilepsy, has followed operation, suggest that the lesions observed and the symptoms relieved were related In those cases where discrete lesions were found in the temporal lobe, either of small space occupying character or of localised sclerosis, it seems likely that these lesions were the major factor in the production or continuance of the epilepsy, and more indirectly in the causation of the personality disorder The fact that with accessible space occupying lesions temporal lobectomy is not necessary, because mere excision of the space occupying le[illegible] generally relieves the epilepsy (Falconer 1954), favours such a view On the other hand, in cases where histological study suggests that the change in the temporal lobe may be only part of a general process, this question remains sub judice, for an alternative explanation may be th[illegible] we have relieved the epilepsy by interrupting important links in the neuronal circuits responsible for the production of a seizure

Case 17 is important in this connection because th[illegible] whole of one cerebral hemisphere was grossly diseased but only a temporal lobectomy was performed, and th[illegible] has apparently relieved the symptoms

This patient, referred by Dr Macdonald Critchley, h[illegible] developed a sudden right sided hemiplegia and aphasia at th[illegible] age of 3 years as a complication of measles Her spe[illegible] gradually returned, but she has since been backward, and gross infantile hemiplegia has persisted From the age [illegible] 4½ years she exhibited frequent psychomotor and grand m[illegible] seizures and became difficult to manage Pneumo enceph[illegible]graphy showed a much reduced left cerebral hemisphere w[illegible] considerable uniform enlargement of the left lateral ventric[illegible] Her clinical picture was thus of a type which nowadays [illegible] often considered for hemispherectomy, but we were chary [illegible] such a radical procedure because there was sparing of [illegible] fields of vision, and we could not tell whether her spe[illegible] functions were still located in the left hemisphere Furth[illegible] our E.E G studies, although they showed widespread abn[illegible]malities in both hemispheres, revealed spike discharges [illegible] in the left temporal region We therefore contented ours[illegible] with a temporal lobectomy, arguing that, if necessary, [illegible] could remove the rest of the hemisphere later The resec[illegible] specimen showed gross atrophy and gliosis of all th[illegible] convolutions and gross sclerosis of the Ammon's horn

Follow up since then has been by correspondence, but th[illegible] patient's father reports that she is seizure free, more amenab[illegible] and progressing better at her studies The girl is evident[illegible] still retarded but has learnt to write in English, which is er a foreign language Two explanations are possible for her mprovement: either the sclerosis of the Ammon s horn ather than the atrophy elsewhere was the epileptogenic rigger or the neuronal circuits underlying her seizures were nterrupted by the lobectomy

The frequency with which improvement took place postoperatively in our cases is greater than in most published series We feel that this is due to our policy of including the uncus and the Ammon s horn (and more recently the amygdala as well) in the tissue excised Certainly it is those regions which generally show the greatest pathological changes (5 of the small macroscopic lesions involved those regions in addition to the 12 cases of sclerosis of the Ammon s horn) The therapeutic results in case 10 in which the temporal lobe was excised in two stages support this view Penfield and Jasper (1954) describe an even more illuminating case which was not benefited by a superficial lobectomy but was relieved when the deeper structures were removed at a second operation

We are now on the threshold of a wide expansion in our knowledge understanding and therapeutic control of this ancient scourge of mankind. Various neurophysiologists have reported that in animals electrical stimulation of the hippocampal and amygdalar regions will produce behavioural changes and confusion similar to those observed in temporal lobe epilepsy in man (Gastaut 1953, Kaada et al 1953 1954 MacLean 1954) Similar disturbances can also be provoked by electrical stimulation of the Ammon s horn (or its vicinity ?) in patients at operation (Passouant et al 1954 Pampiglione Falconer and Mitchell unpublished observations) Our knowledge of the physiological functions of these structures is still very incomplete but it is receiving fresh impetus from these experiments on animals as well as from studies of patients with temporal lobe epilepsy

In pioneering any new form of therapy its sponsors must realise that several years must elapse before its merits can be accurately assessed In the past five years we have investigated many epileptics with temporal lobe seizures and it is only in some of these (probably less than half) that the criterion of a unilateral E.E.G focus or bilateral foci in which one side is predominant, can be upheld In many others evidence from the E.E.G of multiple cortical foci and of subcortical epileptic discharges are found All these have appeared unsuitable for surgery However in view of the grave disabilities shown by patients with severe and intractable temporal lobe epilepsy and their unresponsiveness to drug therapy the published results of temporal lobectomy in suitable cases are very encouraging It is therefore incumbent on us to persevere in this field especially as the operative risks are slight

Further developments are likely to be along the lines of better clinical recognition of this malady, of better understanding of its psychiatric aspects of better standardisation of E.E.G criteria for operation and of better correlation of the various clinical radiological and E.E.G changes in the light of the pathological findings It seems that good results are to be expected in any case of psychomotor ' epilepsy in which the focus is confined to one temporal lobe and major convulsive seizures have been absent or infrequent The prognosis for surgery worsens when grand mal becomes frequent or the focus becomes bilateral Early surgery should always be considered if there is a likelihood of an underlying cerebral tumour In other cases it should be considered if the seizures prove disabling and resistant to medication and especially if a personality disorder develops In many of our patients seizures had been present since early childhood but operation had not taken place until adult life One cannot help feeling that if through greater wisdom and knowledge it had been possible to operate on these patients earlier many years of wasted life would have been avoided

Summary

Of 30 patients with intractable temporal lobe epilepsy submitted to temporal lobectomy 12 became fit-free and 14 others greatly improved as regards their epilepsy 20 were benefited as regards their personality changes 17 markedly so

The historical background to the operation the basis of selection of patients the conduct of the surgical intervention, the various pathological findings, and the therapeutic and incidental effects of the operation are discussed

REFERENCES

Bailey P., Gibbs F A (1951) *J Amer med Ass.* 145, 36[illegible]
— Green, J R., Amador L. Gibbs F A (1953) *Proc. Ass. Res nerv Dis* 31 341
Cairns H, Daniel P Johnson R. T Northcroft G B (1947) *Brit J Surg* War suppl 1 p 187
Earle K M. Baldwin M Penfield W (1953) *Arch. Neurol. Psychiat, Chicago* 69 27
Falconer, M A (1953) *Proc R Soc Med* 46 971
— (1954) *Brit med J* ii 939
— Pond D A, Meyer A Woolf A L. (1953) *J Neurol Psychiat* 16 234
Gastaut, H (1953) *Epilepsia,* 2 59
Gibbs E L. Gibbs, F A Fuster B (1948) *Arch. Neurol Psychiat Chicago* 60 331
Gibbs F A (1951) *J nerv ment Dis* 113 522
Green J R., Duisberg R E H McGrath, W B (1951) *J Neurosurg* 8 157
Hill D (1949) *Congr int Neurol Psychiat* 1 27
— (1953) *Proc R Soc Med* 46 965
— (1955) *Rec Prog Med* (in the press)
Jackson J H (1888) *Brain,* 11 179 Taylor J (1931) Selected Writings of John Hughlings Jackson London; vol i
Jasper, H Pertuisset B Flanigin, H (1951) *Arch Neurol Psychiat Chicago* 65 272
Kaada, B R Andersen P Jansen J jun (1954) *Neurology* 4 48
— Jansen, J jun Andersen, P (1953) *Ibid* 3 884
Klüver H Bucy P C (1939) *Arch Neurol Psychiat. Chicago* 42 979
Lennox, W G (1951) *Neurology* 1 357
MacLean, P D (1954) *J Neurosurg* 11 29
Meyer, A Falconer M. A. Beck E. (1954) *J Neurol Psychiat* 17 270
Meyer V, Yates, A. J (1955) *Ibid* 18, 41
Mitchell W Falconer, M. A Hill, D (1954) *Lancet* ii 626
Morris A A (1950) *Med. Ann. D C* 19 121
Mulder D W., Daly D (195[illegible]) *J Amer med Ass* 150 173
Obrador, S (1953) *J Neurosurg* 10 52
Pampiglione, G (1953a) *Epilepsia,* 2 91
— (1953b) *Proc R Soc Med* 46 974
Passouant, P, Gros, C Cadilhac, J Vlahovitch B (1954) *Rev Neurol* 90 265
Penfield, W (1954) *Brit. J Surg* 41 337
— Baldwin, M. (1952) *Ann Surg* 136 625
— Flanigin H (1950) *Arch. Neurol Psychiat., Chicago* 64 491
— Erickson T C. (1941) Epilepsy and Cerebral Localization London.
— Jasper H (1954) Epilepsy and Functional Anatomy of the Human Brain London
— Rasmussen T (1953) The Cerebral Cortex of Man. New York.
Petit Dutaillis D., Christophe, J, Pertuisset B Dreyfus-Brisac, C (1953) *Sem. Hôp Paris,* 29 3858
Pond D A, Bidwell, B (1954) *Brit med J* ii 1520
Sano K, Malamud, N (1953) *Arch Neurol Psychiat Chicago* 70 40
Scoville W B (1954) *J Neurosurg* 11 64
— Dunsmore R. H Liberson W. T, Henry C E. Pepe A (1953) *Proc Ass Res nerv Dis.* 31 347
Spielmeyer W (1930) *Arch. Neurol Psychiat Chicago,* 23 8[illegible]
Wilson S. A K (1940) Neurology London; vol ii, p 1523.

When society begins to invest academic work with a mystique and to regard the latter-day scholar as a latter-day priest then the university should respond by emphasising the relevance of knowledge to the problems of society, by coming into the market place demonstrating that science is only organised common sense encouraging the study of its applications debunking the expert And when society swings the other way and begins to undervalue pure scholarship to press for quick and tangible results, to let loose the Philistines on the university then the university should respond by withdrawing it should emphasise that the higher learning cannot be justified by profits or popularised without losing some of its precision it should remind society that the scholar must inevitably belong to an *élite* it should assert that there is a timeless quality about some kinds of knowledge Such an attitude as this may sound to be inconsistent and opportunist; but in point of fact for each succeeding climate of opinion such a response as this from the university would be perfectly consistent and anything but opportunist, indeed, it would put the university perpetually in opposition, as it were to the currents on the surface of society And I believe that is as it should be"—ERIC ASHBY D.SC *Listener*, March 17, 1955 p 468

BLOOD-AMMONIUM LEVELS IN LIVER DISEASE AND "HEPATIC COMA"

ELIZABETH A PHEAR
B A. Camb , Ph.D Lond
RESEARCH ASSISTANT

SHEILA SHERLOCK
M.D Edin , F R C P
PHYSICIAN AND LECTURER IN MEDICINE

W H J SUMMERSKILL
M.A , B.M Oxfd, M R C P
MEDICAL REGISTRAR AND TUTOR

POSTGRADUATE MEDICAL SCHOOL OF LONDON

NEUROLOGICAL complications have been induced in patients with hepatic cirrhosis by the administration of large doses of ammonium chloride (van Caulaert et al 1932, Kirk 1936, Phillips et al 1952), and high blood-ammonium levels have been found during episodes of spontaneous hepatic coma complicating cirrhosis (Traeger et al 1954, Riddell and McDermott 1954, Sherlock et al 1954) In this paper we report blood-ammonium levels in a representative series of patients with liver disease with and without neurological changes An attempt has been made to determine the mechanism of the changes in blood-ammonium levels, and to assess the usefulness of blood-ammonium estimations as a routine clinical procedure

Case-material

We studied 66 patients with liver disease, 33 of whom showed neurological changes (table I), and 33 control subjects The latter were hospital staff and patients with chronic pulmonary or cardiac disease who had no clinical evidence of liver disease and normal liver-function tests

Methods

Neurological changes were similar, regardless of the ætiology of the liver disease The neurological status was graded as 0 (normal), 1 (minor disorder of consciousness and the motor system), 2 (gross disorder of consciousness and the motor system), or 3 (coma) Mental changes, which included apathy, confusion, inappropriate behaviour, and excitement, were regarded as the more sensitive index The common motor system signs were "flapping" tremor of the outstretched hands, altered muscle tone and tendon-reflexes, ankle clonus and extensor plantar responses

Impairment of liver function was assessed by clinical history, presence of jaundice and ascites, and serum-bilirubin and serum albumin levels

Extent of the portal venous collateral circulation was assessed clinically, by barium swallow, œsophagoscopy, and percutaneous transplenic venography (Atkinson et al 1955)

Venous catheterisation was used in 28 subjects to estimate the blood-ammonium levels in the hepatic and renal veins In the group without liver disease, readings were made when catheterisation was otherwise indicated for a necessary assessment of cardiovascular, metabolic, or renal function In 7 instances portal vein blood was obtained from abdominal-wall-collateral veins or at operation

TABLE I—PATIENTS STUDIED

Disease	No of cases	No with neurological complications
Acute icteric virus hepatitis	16	8
Portal cirrhosis	42	20
Biliary cirrhosis	5	2
Obstruction to hepatic veins	1	1
Low-output cardiac failure with hepatic necrosis	1	1
Obstructive jaundice with hepatic malignant deposits	1	1
Extrahepatic obstruction to portal vein	2	0

Blood ammonium levels were determined by Conway's (1950) microdiffusion method

0 5 ml of blood was delivered from a calibrated straight bore pipette into the outer chamber of a scrupulously clean Conway unit containing 1 ml of saturated potassium carbonate. A well greased lid covered the unit, and the ammonia liberated by the alkali was absorbed by 0 7 ml of $\frac{N}{4000}$ HCl in the central chamber during 15 minutes' incubation Using Tashiro's indicator, residual HCl was titrated with $\frac{N}{4000}$ Ba(OH)$_2$ delivered from a microburette Results were calculated as described by Conway and expressed in microgrammes of ammonium nitrogen per ml of blood

There is probably no measurable free ammonium in normal circulating blood (Conway 1950) but it is liberated very rapidly after shedding The observation of Conway and Cooke (1939) and Strehler et al (1942) that carbon dioxide prevents the liberation of ammonia was not confirmed, and 6 serial estimations were made on each blood sample in air These represent points on an asymptotic curve of ammonium concentration (White et al 1955)

TABLE II—BLOOD AMMONIUM LEVELS DETERMINED IN HEALTHY PEOPLE BY MODIFICATIONS OF CONWAY PROCEDURE

Reference	Preservative	Time between shedding and introduction into unit	Diffusion time (minutes)	No of observations	Mean blood ammonium nitrogen (µg per ml)	S.D.
Mann et al (1954)	None	30–40 min	60	21	1 14*	0·37*
McDermott and Adams (1954)	None	"Rapid"	10	10	0 61	0·10*
Singh et al (1954)	CO$_2$ and low temperature	10 min	?	34	0 11	0·03
Traeger et al (1954)	CO$_2$	"Rapid"	60	23	1 2	0·43*
Present work	None	40 sec	15	33	0 77	0·12

* Calculated from histograms given in text

Each estimation was timed from the moment of beginning the collection of blood until an aliquot was pipetted into the chamber Conway found progressive liberation of ammonium from exposed blood, and it is therefore imperative to pipette the blood rapidly It was possible to introduce an aliquot into the chamber in less than 40 seconds after withdrawal. Although zero time ammonium may be most significant, estimation of this depends on back extrapolation from only two points By 3 minutes, ammonium concentration had reached a maximum, and this value was chosen as most reliable and representative We did 3 estimations before and 3 after this time, and we have considerable confidence in this value, although values after the maximum had been reached occasionally deviated by as much as 0 1 µg per ml

Table II compares values obtained in healthy people with those obtained by other workers using the same method Large discrepancies are observed either when standards are not run simultaneously or when the blood is not pipetted immediately Older methods, which give very variable values for blood ammonium, are well reviewed by Bénard and Gajdos (1952)

Blood-ammonium Levels in Virus Hepatitis and Cirrhosis

In control subjects the mean peripheral-vein blood ammonium level was 0 77 µg per ml of ammonium nitrogen, and the value never exceeded 1 00 µg per ml The mean hepatic-vein blood ammonium level was 0 74 µg per ml (fig 1)

In virus hepatitis the mean peripheral vein blood-ammonium levels were higher than in normal subjects

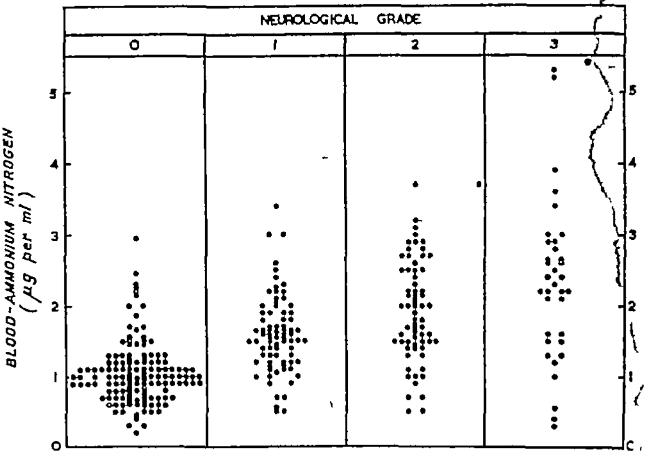


Fig 2—Blood-ammonium levels related to grade of neurological disability Solid circles neurological signs present or past ; open circles no neurological signs.

but this was due to the high levels found in patients with neurological complications no deviation from normal being found in uncomplicated cases (fig 1) The blood ammonium level was always higher in the hepatic vein than in the peripheral vein

In cirrhosis of the liver the mean peripheral vein blood ammonium level was raised slightly in patients without neurological complications and significantly in patients with them. The mean level in the peripheral vein exceeded that in the hepatic vein (fig 1)

In both hepatitis and cirrhosis the scatter was wide, and 3 patients with hepatitis and 2 with cirrhosis all with neurological complications showed little or no rise in the blood ammonium level.

In 6 of 7 subjects the blood ammonium level was much higher in the portal vein than in the peripheral vein The other blood sample came from a gastric vein High values were also common in the right renal vein (fig 1)

These observations support the conclusions previously reported (Kirk 1936, White et al 1955) that portal blood and to a lesser extent renal blood are important sources of peripheral vein ammonium In patients with severe virus hepatitis the failing liver allows ammonium to pass into the peripheral blood. In patients with cirrhosis in addition to impaired hepatic function the collateral circulation delivers portal vein blood directly to the peripheral blood-stream before it can be metabolised by the liver

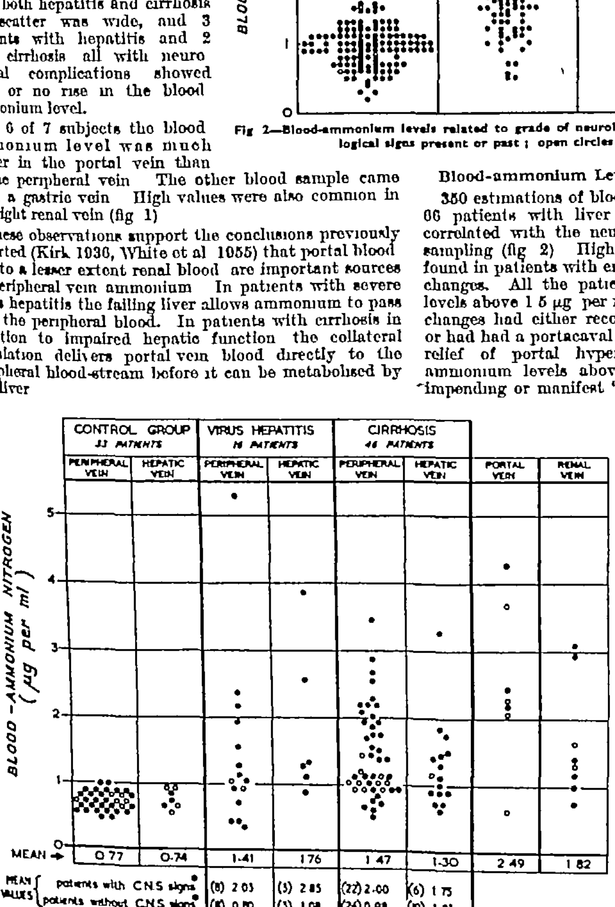


Fig. 1—Blood-ammonium levels in peripheral hepatic, renal and portal veins in controls and in liver disease.

Blood-ammonium Levels and Neurological Status

350 estimations of blood ammonium were made in the 66 patients with liver disease, and the values were correlated with the neurological status at the time of sampling (fig 2) Higher blood ammonium levels were found in patients with either present or past neurological changes. All the patients who had blood ammonium levels above 1 5 μg per ml but no objective neurological changes had either recovered from these complications or had had a portacaval anastomosis constructed for the relief of portal hypertension Those with blood ammonium levels above 2 0 μg per ml had either impending or manifest "hepatic coma" (*portal systemic encephalopathy*) at the time of sampling The proportion of patients with high levels rose as the neurological condition deteriorated However about 10% of estimations in each of the grades 1 2, and 3 were within the normal range

In individual patients the correlation of the blood ammonium levels with fluctuations in the neurological status was variable but never exact Estimations in 14 patients in terminal hepatic coma showed wide fluctuations unrelated to the neurological condition (fig 3) Of 38 estimations, 8 were within the normal range but in no patient was the blood ammonium level consistently normal This demonstrates the unsuitability of blood ammonium estimations in diagnosis, prognosis and assessment during terminal hepatic failure

In contrast 2 patients were studied with cirrhosis of the liver complicated by portal vein thrombosis and an extensive collateral circulation but only moderate impairment of

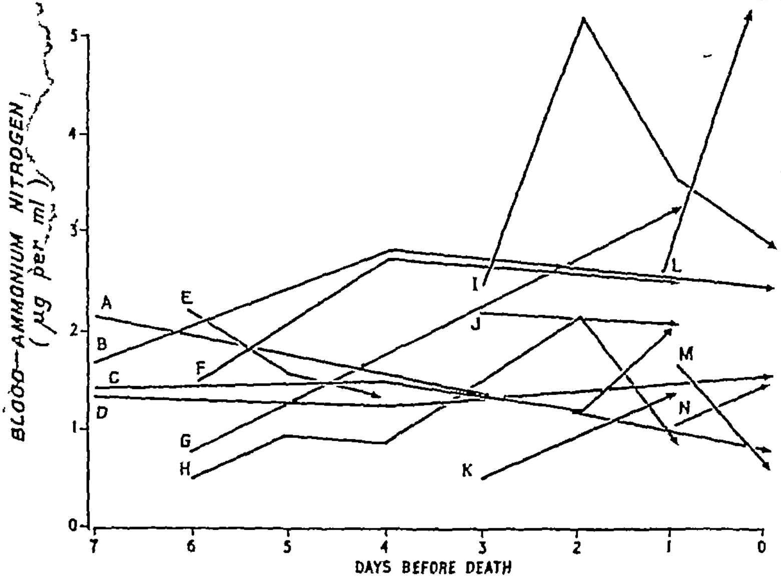


Fig 3—Blood-ammonium levels in 14 patients during last week of irreversible hepatic coma.

liver function Raised blood ammonium levels and neurological signs were always found

In case 1 (fig 4) the height of the blood ammonium correlated approximately with the severity of the neurological changes and with the therapeutic intake of nitrogenous substances (dietary protein, *dl*-methionine, and ammonium chloride) When ammonium chloride was administered, the blood ammonium level was raised for six days before neurological deterioration took place Eventually, on the twelfth day, the patient was still showing severe neurological changes, but the blood ammonium level was lower than on the previous two days. On the second occasion that ammonium chloride was given, the neurological status and the blood ammonium level improved simultaneously Worsening of the neurological status by oral *dl* methionine was associated with a rise in the blood-ammonium level

In case 2 (fig 5) there was again a fair correlation between the neurological condition and the blood ammonium level. During the first three weeks in hospital, restriction of dietary protein was followed by clinical improvement and a fall in the blood ammonium level As in case 1, therapeutic administration of ammonium chloride caused the blood ammonium level to rise before clinical deterioration took place, and again recovery coincided with a fall in the blood ammonium level. Following oral *dl* methionine, a relapse was associated with a rise in the blood ammonium level.

Blood-ammonium levels cannot be used to assess the long-term prognosis of patients with chronic liver disease and neurological complications We have observed consistently raised blood-ammonium levels for periods of three to ten months in 4 patients with cirrhosis and an extensive collateral circulation without any deterioration in neurological or hepatic function

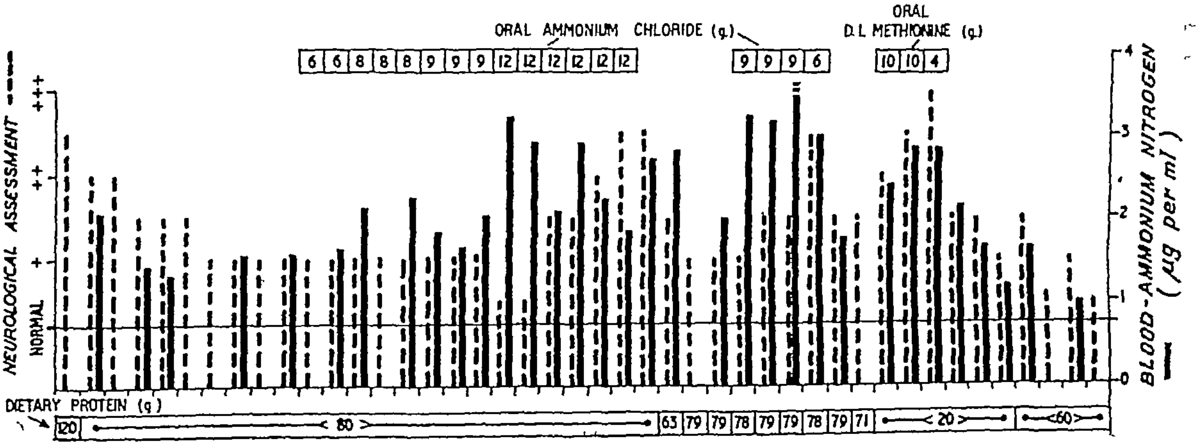


Fig 4

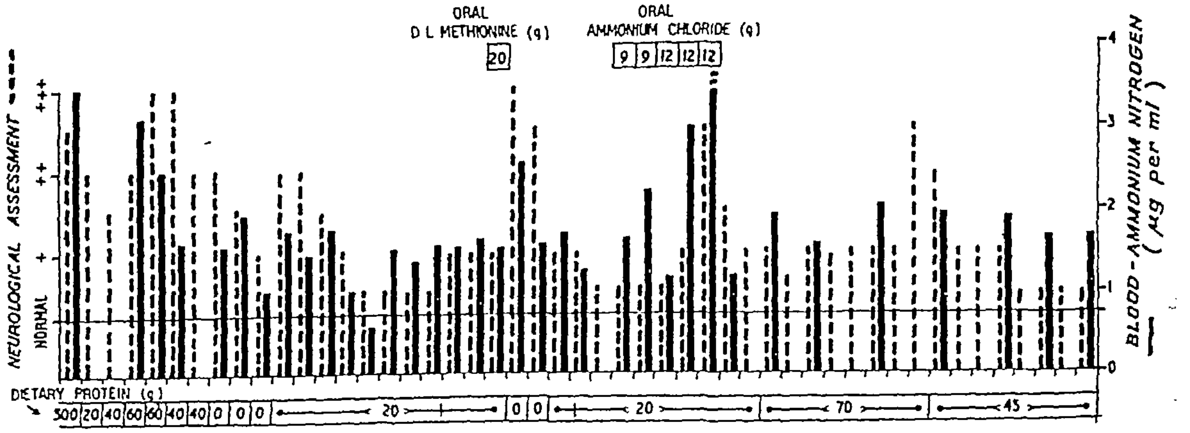


Fig 5

blood-ammonium levels in 2 patients with cirrhosis and persistent although variable neurological changes

TABLE III—BLOOD-AMMONIUM LEVELS IN PATIENTS WITH PORTAL-VEIN OCCLUSION AND GOOD LIVER FUNCTION

Case no	Sex	Age (yr)	Diagnosis	Serum bilirubin (mg per 100 ml.)	Serum albumin (g per 100 ml)	Blood ammonium nitrogen (µg per ml)
3	F	8	Congenital obliteration of portal vein	0 7	3·6	0 8
4	M	16	Pylephlebitis portal vein thrombosis	0 7	4 9	0 9
5	F	49	Cirrhosis thrombosed portal vein	0 9	3 7	0 8
6	M	55	Cirrhosis thrombosed portal vein	0 7	4 6	1 1
7	M	25	Cirrhosis thrombosed portal vein	1·0	4 1	1·0

Blood ammonium Levels in Relation to Portal Collateral Circulation and Hepatocellular Function

In 5 patients there was evidence of an extensive portal systemic shunt the liver was normal in 2 and in 3 there was histological evidence of cirrhosis, but liver function tests were normal (table III) Blood ammonium levels were not raised and there was no neurological change even after feeding increased dietary protein, methionine or ammonium chloride An extensive portal-systemic shunt is therefore not necessarily accompanied by either raised blood ammonium levels or neurological changes we have never seen these complications with a histologically normal liver, and there are no reports of them in the literature Blood-ammonium levels may be high in the absence of an extrahepatic portal collateral circulation in patients with severe virus hepatitis (fig 1)

Between these extremes, high blood ammonium levels may be found in patients with extensive portal collaterals and moderate hepatocellular failure and in patients with more severely impaired liver function and smaller collateral circulations. Therefore abnormal hepatic function is essential before the blood ammonium level rises, and this rise is greatly accentuated by the presence of a portal systemic collateral circulation

Discussion

Estimation of blood-ammonium has the disadvantage of uncertain specificity In fasting subjects without liver disease there is probably no measurable free ammonium in the circulating blood (Conway and Cooke 1939) Values represent points on ascending curves of ammonium liberation and include ammonium liberated during the breakdown of certain compounds in blood as well as "free" ammonium. Technical difficulties account for the different values obtained in various laboratories using the same basic Conway procedure (table I) Each laboratory must therefore determine its own normal value remembering that inaccuracies increase with the time allowed for evolution of ammonium after the shedding of blood The impossibility of preventing this liberation of ammonium from blood after it has been shed is a disadvantage and timed pipetting of blood into the Conway chamber must be done at the bedside The rapid serial estimations used in the present work reduce inaccuracies inherent in microtitration of ammonium but the procedure may be unreliable in the hands of laboratory assistants inexperienced in the method

Previous investigations have been confined largely to patients with cirrhosis, and the total number of estimations published is small Raised blood ammonium levels have been attributed to portal systemic shunting (Kirk 1936 Singh et al 1954 Mann et al 1954) but accurate assessment of the portal circulation has not been attempted. In our patients transplenic portal venography was used to assess the extent of the collateral circulation and it has been shown that mere shunting of portal blood with a high blood ammonium level into the systemic circulation is insufficient to raise the peripheral blood ammonium level if liver function is normal In virus hepatitis Traeger et al (1954) found normal blood ammonium levels in 5 patients, and Riddell and McDermott (1954) found a high blood ammonium level in 1 comatose patient In the present series a high level was found in 7 of 18 patients with virus hepatitis, of whom 6 had portal-systemic encephalopathy

Patients with neurological signs have a higher mean blood ammonium level than those with uncomplicated liver disease This finding applies to all groups regardless of ætiology Furthermore, when a large series is studied there is some association between the blood ammonium level and the severity of the nervous disorder, but there are exceptions These observations however can rarely be applied to individual patients. In acute terminal cases where death in coma is due to liver failure, no relation between blood-ammonium levels and the neurological changes is found although the blood ammonium may be raised this is not always above normal and varies widely In patients with persistent neurological signs on a controlled diet there is often a correlation between blood ammonium level and neurological status all these patients having large portal systemic collateral channels and only slight impairment of liver function They form a fascinating but restricted aspect of the problem of hepatic coma

The clinical value of blood ammonium estimation is therefore limited If the level is above 2 µg per ml (twice the upper limit of normal) the patient will be either suffering or recovering from the neurological complications of liver disease If it is below 2 µg, few useful conclusions can be drawn in diagnosing neurological changes and coma either in a patient with known liver disease or where evidence of liver disorder is equivocal Early diagnosis is made more readily by the clinical picture of personality change, "flapping" tremor on sustained posture, increased tendon reflexes with rigidity and usually flexor plantar responses (Adams and Foley 1953) The estimation of blood-ammonium has no place in prognosis and is not a practical test of liver function

Nevertheless the blood ammonium level in liver disease is of considerable theoretical interest In patients with liver disease a high blood ammonium level is mainly of intestinal origin ammonium reaching the systemic circulation by portal systemic venous channels and/or passing through a damaged liver Ammonium may be of importance in the pathogenesis of hepatic coma When ammonium chloride is given by mouth or intravenously to some patients with cirrhosis, the characteristic neurological changes of liver disease are reproduced (Phillips et al 1952, Seegmiller et al 1954) However these neurological changes can occur without significant raising of the blood ammonium level, and this discrepancy demands consideration From the clinical standpoint disadvantages have already been mentioned On theoretical grounds it might be possible for intracellular intoxication with ammonium to occur in the brain when normal peripheral vein blood ammonium values are found by current unsatisfactory techniques Alternatively, blood ammonium levels may reflect only the amount of portal venous blood reaching the systemic circulation without being adequately metabolized by the liver Portal blood might contain some toxic factor at present unknown Identical neurological changes can be precipitated by administering oral methionine without producing a constant rise in the blood ammonium level (Phear et al 1955) The relation of blood ammonium levels to liver coma might thus be similar to the relation of blood urea levels to clinical uræmia (Singh et al 1954): in both cases a correlation can be established, but in neither is the relationship causal

Summary

350 blood ammonium estimations were made on 66 patients with liver disease of whom 33 showed neurological complications, including hepatic coma

High blood-ammonium levels could be related to impaired hepatocellular function and a portal-venous collateral circulation Raised levels were found in some patients with severe virus hepatitis without a collateral circulation, but extrahepatic portal-venous obstruction with good liver function were compatible with normal values In cirrhosis raised levels could be attributed to both, the collateral circulation and impaired liver function

In patients with neurological changes, the blood-ammonium levels were usually correlated with the severity of the neurological disturbance, but 10% of values were in the normal range regardless of the degree of neurological involvement Levels above 2 µg per ml (twice the upper limit of normal) were invariably associated with neurological changes

The technique of estimating blood ammonium levels has both theoretical and practical disadvantages It cannot be recommended as a routine method of diagnosing the neurological complications of liver disease (particularly hepatic coma) or of assessing prognosis Once the clinician is familiar with the clinical sequence it is unmistakable

The relation of ammonium toxicity to hepatic coma is briefly discussed

We wish to thank the Medical Research Council for a maintenance grant to one of us (E A. P), Dr Laurens P White for help in evolving the method of estimating blood-ammonium, and Miss Marjorie Cole, B SC, for biochemical assistance

REFERENCES

Adams R D Foley, J M (1953) *Res Publ Ass nerv ment Dis* 32, 198
Atkinson, M, Barnett E, Steiner, R E, Sherlock, S (1955) *Quart J Med* 24, 77
Bénard H Gajdos, A (1952) Les fonctions hépatiques Paris p 173
Conway E J (1950) Micro diffusion Analysis and Volumetric Error London
— Cooke R (1939) *Biochem J* 33, 457
Kirk, E (1936) *Acta med scand* suppl 77
McDermott, W V jun, Adams R D (1954) *J clin Invest* 33 1
Mann J D Bollman, J L, Huizenga K A, Farrar, T Grindlay, J H (1954) *Gastroenterology* 27, 890
Phear E A Rubner, B Sherlock S, Summerskill W H J (1955) In preparation
Phillips, G B Schwartz, R, Gabuzda G J jun Davidson, C S (1952) *New Engl J Med* 247, 239
Riddell A G McDermott W V (1954) *Lancet* i 1263
Seegmiller J E Schwartz, R, Davidson, C S (1954) *J clin Invest* 33, 984
Sherlock, S Summerskill, W H J, White, L P, Phear E A (1954) *Lancet*, ii 453
Singh, I D, Barclay J A Cooke W T (1954) *Ibid*, i, 1004
Strehler E Haas, J, Rupp, F (1942) *Biochem Z* 313, 170
Traeger H S, Gabuzda G J jun Ballou, A N, Davidson, C S (1954) *Metabolism* 3 99
van Caulaert C, Deviller C, Halff (1932) *C.R Soc Biol. Paris* 111, 739
White L P, Phear E A Summerskill W H J, Sherlock, S (1955) *J clin Invest* 34, 158

ACHALASIA OF THE CARDIA IN ADOLESCENTS PRESENTING WITH RESPIRATORY SYMPTOMS

DEWI DAVIES
M.D Lond, M.R C.P
SENIOR MEDICAL REGISTRAR

JOHN C ROBERTS
M D Lond, M R C P
PHYSICIAN

HAREFIELD HOSPITAL, MIDDLESEX

USUALLY the diagnosis of achalasia of the cardia is made in adults presenting with difficulty in swallowing and regurgitation of food On questioning, they often admit to some difficulty in swallowing for many years, but the early symptoms are so slight and the deterioration so grad[illegible] that they do not seek medical advice for a lo[illegible] Even these cases, presenting in adult life, [illegible]lation about the time of development of the disorder and raise the possibility that it may b congenital

It is not uncommon, however, for the discovery to b made in childhood Thus Olsen et al (1953), reviewin 601 cases, found 17 to be under the age of 16 at the tim of diagnosis, the youngest being 2 years old. In 24 o them the symptoms had developed before the age of 10 Such children grow up with a disordered swallowin mechanism and may not realise how much they depar from the normal They often acquire habits to overcome their difficulty, and may take gulps of fluid, breathe deeply, or crouch forwards while eating

Andersen et al (1953) found pulmonary complication in 63 of their 601 cases In most of these the compli cations were preceded by dysphagia But it has bee recognised for a long time that achalasia may be mistake for respiratory disease, particularly in children (Moersc 1929) Belcher (1949) collected 34 cases with pulmonar complications from his own experience and from th literature In 6 of these the œsophageal disturbance wa virtually silent, not arousing complaint by the patient and in some others dysphagia was slight

The purpose of the present paper is to emphasise aga that patients with achalasia can present with respirator disease from spill over of œsophageal contents This i particularly so in children and adolescents, and con siderable vigilance may be required to arrive at the caus of the trouble

Illustrative Case-reports

Case 1 —At the age of 13 this boy coughed up blood o two occasions, and investigation revealed no cause for th At the age of 14, and in the summer, he developed a dr cough During the following winter he began to produc purulent sputum, but this again cleared with the advent o summer He was then admitted to hospital, at the age of 1 as a possible case of bronchiectasis While being investigate for this, he was observed to take a long time over his foo and to swallow water after each mouthful A history o indigestion was obtained, and it appeared that for abou two years he had had some difficulty in getting food dow He had developed the habit of gulping fluids with h meals

On clinical examination no gross abnormality was foun Radiography of nasal sinuses and chest was normal, and were bilateral bronchograms A barium swallow show achalasia of the cardia with œsophageal dilatation and pylor spasm

After dilatation of the cardia with a Negus hydrostati bag, the cough cleared and swallowing improved At the e of two years a barium swallow passes down the œsophagu into the stomach without any suggestion of obstruction, an the lumen has returned to normal No further treatment h been required

Case 2 —A boy of 14 lived in a caravan on a fa ground Neither he nor his parents could give a prec history

At about the age of 10 he swallowed some petrol, he h some cough and vomiting afterwards, but his symptoms we not severe and soon cleared At about the age of 12 he had cough with vomiting for three or four days and spent a night in hospital At the age of 13, and about a year bef admission, he had pneumonia He had fever, right sided ch pain, cough, and vomiting Cough with mucoid sput persisted after this, and his breathing became rather no Three weeks before admission he became ill again with fev right-sided chest pain, cough, and frothy sputum He w admitted to hospital with a provisional diagnosis of pneumo complicating bronchiectasis

On admission his temperature was 103°F and his breath was rapid The mediastinum was displaced a little to t right, and there were signs of consolidation at the right ba He had marked polymorph leucocytosis, and his mucopuru sputum gave a growth of *Hæmophilus influenzæ*

The response to penicillin was rapid During recovery vomited while doing postural tipping Radiography of chest showed a little persistent consolidation at the right b with widening of the upper mediastinal shadow A bar swallow confirmed the presence of considerable dilatatio the œsophagus and constriction at the cardia. After a short period the sphincter relaxed and allowed a fair flow of barium into the stomach. The boy then admitted that food tended to stick at the lower end of his sternum, and that he could help it down by breathing deeply Bronchography showed no abnormality

His symptoms were relieved by Heller's operation. The appearances at operation and during barium swallow confirmed the diagnosis of achalasia. When seen at Henley Regatta eighteen months later, he was symptomless.

Case 3—In 1944 at the age of 18 this patient spent three months in a military hospital with severe cough, copious bloodstained sputum retrosternal pain, and vomiting after food. Bronchitis was diagnosed His symptoms recurred and he was invalided from the Army in 1945 with a diagnosis of bronchiectasis. He spent several periods in hospital after this.

In 1947 he still had a troublesome cough and produced 3 or 4 oz. of foul sputum daily He complained of some vomiting particularly during the bouts of coughing and he also had some difficulty *in swallowing solid food* In October 1947 his bronchiectatic left lower lobe was removed. His cough and sputum then improved, but dysphagia persisted A diagnosis of achalasia of the cardia was made in December 1947 Dilatation with mercury bougies only produced a little relief so Heller's operation was eventually done Four years later he had a slight cough with a little purulent sputum. A little dysphagia persisted and a barium swallow still showed some hold up at the cardia.

This patient's chest X rays showed widening of the upper mediastinum, and in one penetrating film the dilated œsophagus showed clearly through the heart shadow

Discussion

A detailed history usually gives the best clue to the diagnosis but specific questioning about swallowing may be necessary Considerable help is often given by radiography of the chest The changes however are roughly proportioned to the degree of œsophageal dilatation and in case 1 the straight film provided no clue With moderate dilatation the mediastinal shadow is widened from the right border of the heart upwards to the root of the neck The right cardiophrenic angle may also be occluded In the lateral view the trachea is displaced forwards and the mixture of food and fluid in the œsophagus may show up as a mottled density anterior to the vertebral column This was well shown in case 2 With grosser degrees of dilatation the œsophagus encroaches more on the lung field and the diagnosis becomes increasingly obvious Sometimes air in the upper œsophagus may form an area of translucency in the mediastinum in addition to that of the trachea

The spill-over of œsophageal contents into the bronchial tree may produce a wide variety of respiratory disorders, ranging from an irritant cough and a tickle in the throat to pneumonitis abscess, bronchial occlusion bronchiectasis lung fibrosis and lipoid pneumonia Lung shadows with acid fast saprophytes in the sputum may also be mistaken for tuberculosis unless the cultural characteristics and the pathogenicity of the organisms are studied (Breakey et al 1951) These cases show the insidious character of the early symptoms of achalasia which may be accepted by the patient as normal for him The respiratory complication may overshadow the primary pathological process.

We wish to acknowledge our indebtedness to Mr T Holmes Sellors, who operated on cases 2 and 3; and Mr Vernon Thompson, who operated on case 1

REFERENCES

Andersen, H A., Holman, C. B Olsen A. M. (1953) *J Amer med Ass* 151 608
Belcher J R. (1949) *Thorax* 4 44
Breakey A. S., Dotter C T Steinberg I (1951) *New Engl J Med* 245 441
Morrell, H J (1929) *Amer J Dis Child*. 38 204
Olsen A M., Holman, C. B., Andersen, H A. (1953) *Dis Chest* 23 477

PLASTIC APPLIANCES MOULDED DIRECT TO PATIENT

J B BRENNAN
M B Glasg
REGISTRAR IN PHYSICAL MEDICINE WHITTINGTON HOSPITAL, LONDON

PLASTIC orthopædic appliances are, generally speaking lighter cheaper more comfortable and less difficult to make than those of metal and leather and for most purposes they are just as strong and durable

Much research has been required in the development of these fascinating plastics In this country the plastic research unit of the Royal National Orthopædic Hospital has played a leading rôle in this respect (Scales 1950, 1951)

The major impediment to their general use was the necessity of shaping the appliances to previously prepared plaster of paris casts with consequent expenditure of time, skill and money With the introduction last year of applying plastic splints direct to patients (Van Swaay 1954 Brennan 1954) this has been overcome. At the Whittington Hospital this technique has been used to make efficient and comfortable appliances quickly and cheaply for cervical dorsal and lumbar lesions, and a new type of splint for the prevention and treatment of bedsores has also been successfully developed.

Polythene and polyurethane are used in each case They are rendered malleable by simple heating and then applied direct to the patient (Brennan 1954) When cooled the polythene provides the rigidity and strength while the spongy elastic polyurethane serves the dual purpose of heat insulation during application and of forming a very comfortable padding in the finished appliance

Cervical Support

Design—Four pieces of $^1/_8$ inch polythene and $^3/_{16}$ inch polyurethane are cut (fig 1) These are strengthened by superimposing extra polythene strips which coalesce to them during heating The anterior piece consists of a base to rest on the upper part of the chest and a chin piece corresponding in shape and size to the under

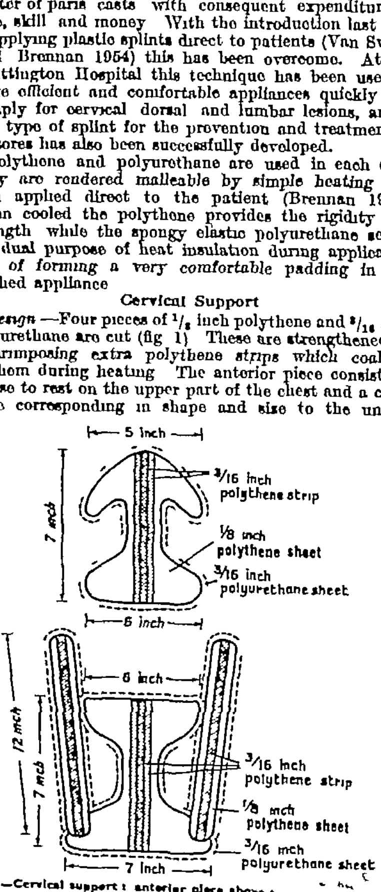

5 inch
7 inch
3/16 inch polythene strip
1/8 inch polythene sheet
3/16 inch polyurethane sheet
6 inch
6 inch
12 inch
7 inch
3/16 inch polythene strip
1/8 inch polythene sheet
3/16 inch polyurethane sheet
7 inch

Fig 1—Cervical support: anterior piece above; shoulder-straps below

The plastics arranged as shown above are in the oven (this applies also to figs. 3 6 ments are average.

surface of the chin and rami of the mandible, the two being joined by a strong narrow strip for the neck The posterior piece is cut in a similar way, the upper end being shaped to fit round and under the occiput The shoulder straps are cut to the required length, and during heating their posterior ends are coalesced to the base of the posterior piece

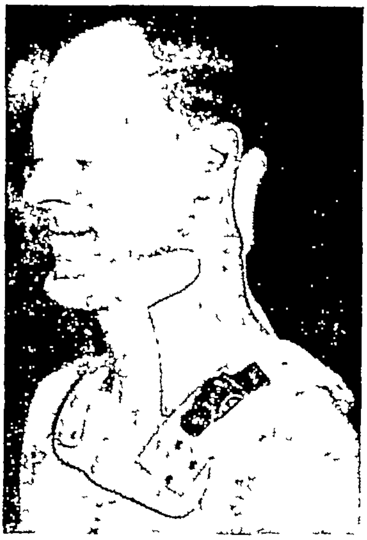
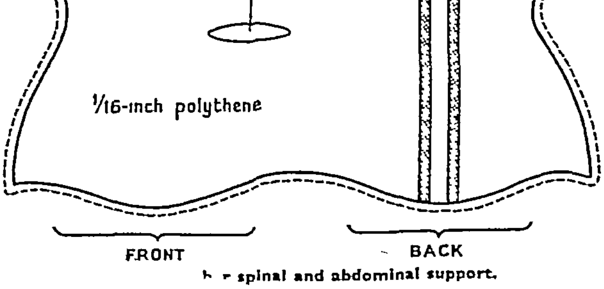


Fig 2—Cervical support in position on patient.

Application —The patient sits with his head and neck in the correct position The heat softened anterior piece is removed from the oven and placed in position Two turns of a crêpe bandage are made under the chin and over the vertex to fix the anterior piece temporarily The posterior piece and its attached shoulder straps are then placed in position, and the bandage is taken round the neck to include both anterior and posterior pieces Bandaging is continued until all the parts are gently moulded to the skin It is not necessary to bandage round the chest to mould the bases and shoulder straps, once the upper parts are fixed in position, these can be moulded with the fingers Within 15 minutes the plastics cool sufficiently to be removable without losing their shape Before this is done, however, the overlap of the two shoulder-straps on the base of the anterior piece should be marked in ink so that they can later be riveted to it in the correct place

Finishing —The shoulder straps are fixed to the anterior piece with bifurcated steel rivets or by welding with an electric soldering-iron The left shoulder strap is next divided near the front, and the separated pieces are joined again with a 1 inch buckle and a leather strap The appliance is then ready to wear It is put on by springing apart the cut polythene shoulder strap and slipped on sideways from right to left into position The leather strap and buckle are fastened, and the appliance is in place (fig 2) The patient requires no assistance to put it on or remove it

Comments —This appliance allows a small amount of cervical movement, but it is within the painless range in most cases, and flexion, usually the most undesirable movement, is entirely prevented The $^3/_{16}$ inch polyurethane padding allows the patient to chew and swallow comfortably Almost any degree of immobility can be obtained by modification of this design For example, a semicircular strip of the plastics may be moulded round the right side of the neck and riveted to the anterior and posterior pieces Again, the chin-piece may be extended backwards on both sides to overlap the occipital part of the posterior piece and be riveted to it The appliance, being moulded close to the skin, is inconspicuous and causes little self-consciousness The finished appliance weighs 7–12 oz, and the materials cost from 6s to 11s With a little practice these cervical supports can be made by a physiotherapist or a technician in less than an hour without assistance



spinal and abdominal support.

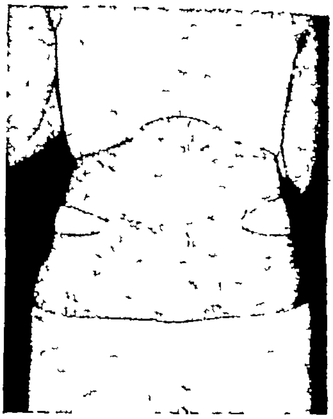


Fig 4—Lumbar spinal and abdominal support of $^1/_{16}$ inch polythene with extra polythene strip forming pelvic hoop. Weight 12 oz.

Spinal Support

Design —The plastics are cut in one piece (fig 3) from $^1/_{16}$ inch or $^1/_8$-inch polythene and $^3/_{16}$ inch polyurethane and strengthened with strips of polythene where required With experience full length spinal braces can be produced A cervical support, as described above, can be added to the brace if required To assist moulding, an elliptical window is cut out above the iliac crest on the closed side of the support (fig 4), if this is not done, wrinkles will develop at the waist

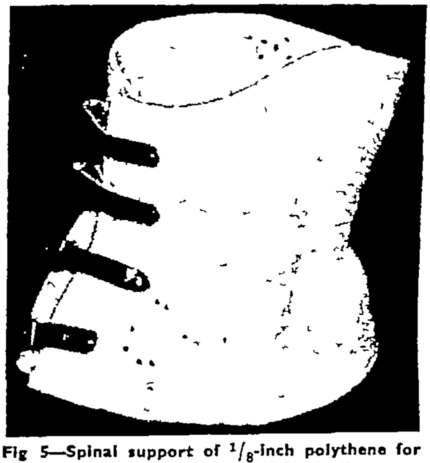


Fig 5—Spinal support of $^1/_8$-inch polythene for patient with chronic back pain due to degeneration of intervertebral discs L1–L4 Upper border of jacket is just below breasts anteriorly and inferior angles of scapulæ posteriorly Weight 1 lb 12 oz.

Application —The patient stands in optimal posture with his arms abducted to 90° If the abdomen is prominent it should be bound firmly before the materials are applied The sheet of plastics is then wrapped round and held in front by an assistant, while the operator ensures that it is correctly positioned It is then fixed in place with a 3 inch crêpe bandage applied with just enough tension to mould it correctly The patient can then lower his arms The mould is taken off after 15–20 minutes and set aside to cool and harden further After 10 minutes it is reapplied to the patient and the fitting is checked An excess or overlap is marked in ink for future removal

Finishing —A row of 1 inch straps and buckles is provided along the open end (fig 5)

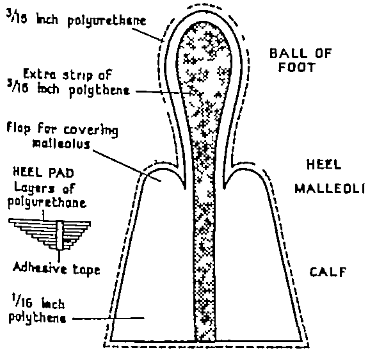
Comments —The weight of these appliances will vary widely with their size, the thickness of the polythene and the number of strengthening strips used. A $^1/_{16}$ inch polythene corset for lumbar and abdominal supp reighs about 10 oz, and a full length $^1/_8$ inch polythene pinal brace for dorsal-spine lesions about $2^1/_2$ lb or a ittle more. Cost will therefore vary roughly from 10s o 35s

Bedsore Splints

The great difficulty in treating bedsores is to keep pressure off the ulcerated areas and so to allow local treatment to take effect I believe that supports made of polythene and polyurethane will be of immense value in treating bedsores Two examples are given of splints designed to provide complete and continued relief from pressure

Heel-sore Splint

Design—Polythene $^1/_{16}$ inch and polyurethane $^3/_{16}$ inch are used strengthened with a strip of $^3/_{16}$ inch polythene (fig 6) While the plastics are being heated a pad of polyurethane about $2^1/_2$ inches thick is taped to the heel and tapered over the distal part of the Achilles tendon (fig 6) When the splint is being moulded this pad, being t and elastic is compressed evenly and gives a smooth anded mould The same pad can be used for each case.



$^3/_{16}$ inch polyurethane
BALL OF FOOT
Extra strip of $^3/_{16}$ inch polythene
Flap for covering malleolus
HEEL
HEEL PAD Layers of polyurethane
MALLEOLI
Adhesive tape
CALF
$^1/_{16}$ inch polythene

Fig 6—Heel-sore splint

Application—The plastics are applied in position from e calf to beyond the toes and moulded by bandaging und the limb and over the pad The splint is removed ter 10 minutes and set aside to cool to room tempera re The pad is taken off the sore

Finishing—The splint is finished with leather straps d buckles. When it is applied to the patient it is seen at, the splint having been moulded over the pad an r gap is left below the heel so that no pressure whatso er acts on the sore The heel cannot fall down into the p because the foot is kept dorsiflexed by the diagonal raps (fig 7)

Comments—With this design the pressure previously pplied to the heel is distributed over the soft bulk of e calf muscles By bringing the plastics above the es during moulding the bed-clothes are prevented from earing on them Finally there is room left for a dressing ough generally the sore will heal spontaneously when lieved of pressure When the splint is discarded it is sually possible to find another patient of similar measure ents for whom it can be used

acral-sore Jacket

Design—Whereas the heel sore splint is easy to ake and when applied requires little attention, it is ifficult to devise a sacral-sore jacket with similar virtues lowever the appliance here described has been found dequate provided the nurses make sure that it stays in osition As with the heel splint the jacket is designed o keep pressure off the sore and to redistribute it over wide area The materials are cut as in fig 8 from $^3/_{16}$ inch olythene and $^1/_2$-1 inch polyurethane for the posterior iece and $^1/_{16}$ inch polythene and $^3/_{16}$ inch polyurethane for the anterior piece A 2 inch overlap of polyurethane is provided below the lower border of the posterior piece and later turned out and pressed on to the outer surface of the heat-softened polythene it then adheres firmly to it thus forming a well padded lower border

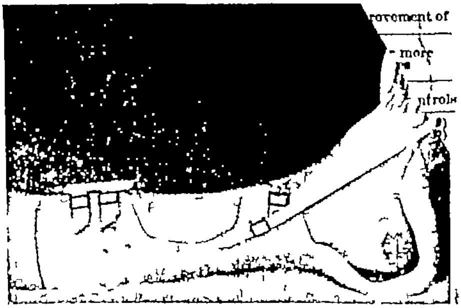
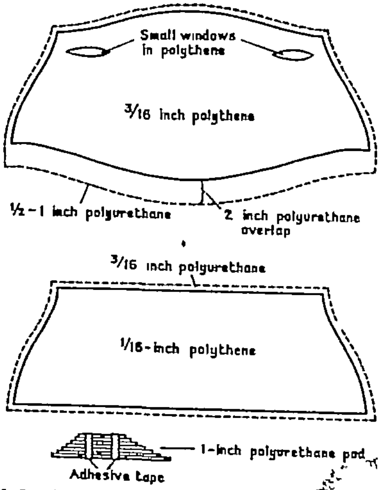


Fig 7—Heel-sore splint in position on patient. Malleolar flaps have not been provided in the prototype splint illustrated here.

Application—Since most patients requiring a sacral sore jacket cannot stand the patient is kept in bed and the jacket is applied in two pieces—anterior and posterior A 1 inch pad of polyurethane is built up from $^3/_{16}$ inch pieces (fig 8) its area being rather larger than that of the sore This pad is laid on the sore, and the heat softened posterior piece is laid over it. The plastics are manually moulded to the area until cooled and hardened this takes about 10 minutes They are then removed the patient is turned over to lie supine, and the anterior piece is laid on and moulded

Finishing—The anterior and posterior pieces are riveted together where their lateral borders overlap A strip 1 inch wide is next cut out down the middle of the anterior piece and four straps and buckles are fitted Ventilation holes are next punched out, and the jacket is ready to wear If the patient is incontinent, oiled silk



Small windows in polythene
$^3/_{16}$ inch polythene
$^1/_2$-1 inch polyurethane
2 inch polyurethane overlap
$^3/_{16}$ inch polyurethane
$^1/_{16}$-inch polythene
1-inch polyurethane pad
Adhesive tape

Fig 8—Sacral-sore jacket: posterior piece above; below

surface of th
being joine ding of the posterior piece
posterior he excretions
being sh ake the patient much
shoulde ng to a minimum All
heatin ck that the appliance
rable after the patient
position for meals If the
, the jacket will inevitably be
have been unable to devise any
of preventing this
nt in favour of the appliance is that the
an use a bedpan with comfort because the hard
ene takes the pressure of the metal rim of the pan

Discussion

Polythene is an almost ideal material for splints and appliances it is inert, radiolucent, and extraordinarily durable , it moulds easily and accurately , and the splint or appliance has a resiliency which enables it to be sprung apart without breaking as the patient puts it on Almost complete rigidity can, however, be obtained by superimposing strengthening strips which coalesce with the body of the appliance during heating These strips *are placed in such a way that the limb or trunk* is prevented from moving in a direction which is harmful, while allowing some movement in other directions This is often of great physiological value, particularly in limb splints (Brennan 1954)

The key to the technique of direct application to the patient is the polyurethane This plastic both insulates the patient from the heat of the polythene during application and forms a most comfortable padding in the finished support It does not have to be glued to the polythene, because it adheres firmly to it during heating (Brennan 1954) Like polythene, it is radiolucent and inert The ratio of continuous to discontinuous air cells is one of the determining factors in the unique padding properties of polyurethane The plastic is laid first on the limb, and, during application, the wet plaster-of-paris partially penetrates its spongy substance so that when dried the polyurethane is firmly adherent to the plaster This is of particular value in removable plasters Another application for this plastic has been introduced by Dr G H Dobney, who advises the use of simple pads of 1-inch polyurethane in place of orthopædic felt or sorbo rubber for the treatment of selected cases of bedsores Being porous to air this plastic has a distinct advantage over the other materials

Polythene costs 13*s* 2½*d* a lb , and polyurethane 13*s* 10*d* a lb —i e , 13*s* 6*d* per lb of the finished support Since very little material is wasted, the cost of the finished appliance is in direct proportion to its weight, plus an additional few pence for straps and buckles These appliances are thus most economical, particularly because they can often be used again when discarded, by heating till flat and reapplying to another patient

I am indebted to Dr G H Dobney for his kindness in reviewing this paper and for permission to publish My thanks are due to Miss E Mason, of the photographic department of St James's Hospital, Balham , Mr A R Kourik, surgical technician, of the Whittington Hospital , and Mr J H Salmon and the staff of the engineering department of Highgate *Hospital for their help*

U K patent application no 16668/54 has been assigned to the National Research Development Corporation by Dr J T Scales A patent has been applied for by M V Esta Voorschoten Holland covering the use of polyurethane foam and 'Perspex' in combination *Polythene* is made as 'Vitrathene' by Messrs Stanley Smith & Co , Isleworth Middlesex *Polyurethane* is made as Moltopren ' by Kay Brothers Ltd Hurst St Reddish near Manchester *Tubular steel rivets buckles &c* are obtainable from Darwen & Co Ltd. Featherstone Street London E C 1 *Plastic glue* ('Evo Stick 528) can be had from Evode Ltd , Stafford, England

REFERENCES

Brennan J B (1954) *Lancet* ii 948
Scales, J) *J Bone Jt Surg* 32B 60
Nangle, E J Instruments and Apparatus in
urgery Oxford chapter XV
Va 51) *Ann phys Med* 1954 2 101

VITAMIN E IN THE TREATMENT OF PRIMARY DYSMENORRHŒA

E Blanche Butler
M B Wales, M R C O G
REGISTRAR, DEPARTMENT OF OBSTETRICS AND GYNÆCOLOGY
CARDIFF ROYAL INFIRMARY

Edith McKnight
M B , B Sc Glasg , D P H.
STUDENT HEALTH OFFICER, UNIVERSITY OF WALES

WITHIN recent years much has been published on the therapeutic value and physiological effects of vitamin E (α-tocopherol)

Adamstone (1931) first reported that the tocopherols were associated with the development of the vascular system in chick embryos Shute (1942) found that senile vulvovaginitis improved clinically under treatment with vitamin E and biopsy showed that this was due either to the reopening of capillaries or to the proliferation of new blood vessels. As there was a time lag of four weeks, he suggested that the latter explanation was the more likely Favourable results *have also been published of the* use of vitamin E in *Buerger's* disease It was suggested that α tocopherol, by improving the blood supply to the muscles or by promoting a better utilisation of oxygen, relieved the ischæmia which caused intermittent claudication Mason (1942), found that a deficiency of vitamin E caused vascular abnormalities such as stasis, distension, and thrombosis in the vessels of the uterine wall in pregnant rats

We have *found no previous record of the use* of vitamin E in spasmodic dysmenorrhœa This condition occurs chiefly in girls and young women, and in the classical case pain is present just before and at the *onset of the menses* In some cases the pain is so severe that the patient regularly loses a day's work, and in less severe cases working ability may be impaired The cause is uncertain, but one hypothesis is that it is due to muscle ischæmia caused by constriction of the uterine blood-vessels at the onset of the menstrual period If this is correct, relief of pain might be expected from the use of vitamin E, which is reported to relieve vasospasm

Method

Our investigation was made with the cooperation of women students living in the halls of residence of the University of Wales All were between 18 and 21 years of age, some being in their first year of university training, and others in their second or third

At the routine medical examination conducted by the student-health service a careful menstrual history was taken from all the female students, and 100 were chosen who gave a history typical of spasmodic dysmenorrhœa These girls had menstrual periods which were regular and otherwise normal Their general health was good and, so far as could be ascertained, they had no psychological difficulties Vaginal examination to exclude pelvic disorder was not done, because of the age of the students The 100 students were spread over three successive academic years

50 girls were given a course of vitamin E tablets, and the remaining 50 (controls) a similar course of placebo tablets These were provided by the firm which supplied the α tocopherol and of the same size, shape, and colour as the vitamin-E tablets All taking part in the experiment were living under similar conditions as regards study, recreation, and diet

The girls reported to the warden of the hostel ten days before the period was due and were given either vitamin E or the placebo in strict rotation Allocation to the treated and control groups was therefore entirely at random, and bias in assessing the results of the treatment was avoided because we, the assessors, did not know which girls had received the vitamin

The course comprised vitamin E (50 mg t.d.s.) for en days before the menstrual period and for the next our days. This fourteen-day course was repeated for wo menstrual cycles and in some cases for three cycles according to the timing of each girl's menstrual periods during the experiment.

Results

Of the 50 given vitamin E 4 girls reported no pain during menstruation in the first treated period but a recurrence of pain in the second treated period. In 2 of these cases there was improvement again in the third period, whereas in the 2 others pain persisted. In these cases the result in the final treated period under consideration has been accepted.

Results are available at the second month for all 100 girls, but in the third month no results are available for 12 of the treated group and 15 of the controls, because the vacation intervened. The results at the second month are therefore considered first (table I).

Second-month Assessment

Table I is divided into three sections. In section A the symptoms during the menstrual period of the second month are compared with those during the last menstrual period preceding the experiment. In section B the symptoms during the premenstrual phase of the second month are compared with those during the last premenstrual phase which preceded the experiment. In section C the symptoms during both the premenstrual and the menstrual phases of the second month are combined and compared with similarly combined features of the premenstrual and menstrual phases of the month preceding the experiment.

This combined grouping depended on the summation of the Xs in the premenstrual and menstrual periods together. For example cases of "X 2X," indicating discomfort in the premenstrual phase together with slight pain during the menstrual period, were combined with cases of "0 3X" indicating absence of pain in the premenstrual phase but severe pain during the menstrual period. However, of the 19 cases classified in the treated group of section C as "3X" before the experiment began 18 were of the "0, 3X" type.

TABLE II—SECOND MONTH RESULTS

Based on experience in	Percentage showing improvement of			
	One or more stages		Two or more stages	
	Treated	Controls	Treated	Controls
A menstrual phase only	68 (*50*)	18 (*50*)	41 (*49*)	8 (*49*)
B premenstrual phase only	81 (*16*)	30 (*20*)	64 (*14*)	15 (*20*)
C premenstrual and menstrual phases combined	68 (*50*)	22 (*50*)	47 (*49*)	14 (*49*)

Numerals in parentheses show numbers on which the percentages are based—i.e., those who could have improved the required number of stages.

The totals in table I show that whether judged by symptoms in the menstrual phase only or by symptoms in the premenstrual phase only, or by a combination of the two, there was little difference as regards severity of symptoms between the treated and controls before the experiment began.

All the cases tabulated to the left of the zigzag line showed improvement of at least one stage at the end of the second month compared with their staging previous to the experiment. The table is to be read as follows.

In the treated group before the experiment 1 girl had slight discomfort (X) during the menstrual period; at the second month after receiving vitamin E she had no symptoms (improved one stage).

TABLE I—SECOND-MONTH RESULTS

A BASED ON SYMPTOMS DURING MENSTRUAL PHASE ONLY

Pre-treatment category	Treated					Controls					% improved one or more categories		% improved two or more categories	
	2nd-month classification					2nd month classification								
	0	X	2X	3X	Total	0	X	2X	3X	Total	Treated	Controls	Treated	Controls
0														
X	1				1		1			1	100			
2X	5	6	9	1	21	2	2	19	1	24	52	17	24	8
3X	7	8	7	6	28	1	1	3	20	25	79	20	54	8
	13	14	16	7	50	3	4	22	21	50				

B BASED ON SYMPTOMS DURING PREMENSTRUAL PHASE ONLY

Pre-treatment category	0	X	2X	3X	Total	0	X	2X	3X	Total	Treated	Controls	Treated	Controls
0	34				34	30				30				
X	1	1			2						50			
2X	1	2	2		5	1	2	5	1	9	60	33	20	11
3X	2	6	1		9	1	1	1	8	11	100	27	89	18
	38	9	3		50	32	3	6	9	50				

C BASED ON SYMPTOMS DURING PREMENSTRUAL AND MENSTRUAL PHASE COMBINED

Pre-treatment category	0	X	2X	3X	4X	Total	0	X	2X	3X	4X	5X	6X	Total	Treated	Controls	Treated	Controls
0																		
X	1					1		1						1	100			
2X	3	4	7	1	1	16	2		13					15	47	13	20	13
3X	5	3	5	6		19			3	11				14	68	21	42	
4X	1		2	1	2	6			3		5		1	9	67	33	50	33
5X																		
6X	2	1	5		1	9	1		1			1	8	11	100	27	100	18
	12	8	10	8	3	50	3	1	20	11	5	1	9	50				

Sections A and B: 0 free from pain X discomfort; 2X, pain but no disability 3X incapacity requiring rest in bed.
Section C: Summation of Xs in menstrual and premenstrual phases maximum possible pain 6X (see text).

21 girls had slight pain (2X) before the experiment, but at the second month 5 of these were symptom free (improvement of two stages), 6 had only discomfort (improvement of one stage), 9 were unchanged, and 1 was worse (incapacitated)

28 girls were incapacitated during the menstrual period before the trial At the second month 7 of them were symptom free, 8 had only discomfort (two stage improvement), 7 had slight pain but were not incapacitated (one stage improvement), and 6 showed no change

Thus 34 of the 50 treated (68%) showed some improvement compared with only 9 of 50 (18%) of the controls Of a possible 49, 20 (41%) improved two stages (significant improvement) compared with 4 of 49 controls (8%) who could have improved two stages The differences between the treated and controls are statistically significant Variations in the proportions showing improvement in the different severity groups are shown in the last two columns of the table

The tabulations of sections B and C are to be interpreted similarly and the principal results are summarised in table II

Tests of significance were applied to all the differences between the treated and controls, and in each case the difference was most unlikely to have arisen merely by chance

In every comparison the improvement shown by the treated was superior to that shown by the controls, and the last two columns of table I show that, in the treated, improvement was greater where the assessment before the trial was most severe

Third month Results

Before analysing the symptoms reported at the third month it was necessary to consider the effect of losing 12 girls from the treated and 15 from the controls If, for example, the defaulters from the treated had all been severe cases, but the defaulters from the controls only the mild cases, this might have invalidated the final comparison In the event, however, no significant difference was found between the pre trial assessments of the defaulters of the two groups, whether based on premenstrual, menstrual, or combined assessments.

TABLE IV—THIRD MONTH RESULTS

Based on experience in	Percentage showing improvement of			
	One or more stages		Two or more stages	
	Treated	Controls	Treated	Controls
A menstrual phase only	76 (*38*)	29 (*35*)	59 (*37*)	14 (*35*)
B, premenstrual phase only	91 (*11*)	29 (*14*)	82 (*11*)	14 (*10*
C, premenstrual and menstrual phases combined	76 (*38*)	29 (*35*)	62 (*37*)	20 (*3*

Numerals in parentheses show numbers who could have improved to the specified extent

Table III presents the analysis of the third month results and is to be interpreted in the same way as table I. The results are summarised in table IV

Improvement during the menstrual phase was shown by 76% of the treated and only 29% of the controls; 59% of the treated improved two stages as against only 14% of the controls

Only 11 of the treated and only 14 of the control had symptoms during the premenstrual phase before the experiment started 10 of the former (91%) but only 4 of the latter (29%) showed premenstrual improvement after three months' treatment

On assessment during the premenstrual and menstrual phases combined, 76% of the treated as against only 29% of the controls showed improvement 62% of the treated but only 20% of the controls improved two stages

TABLE III—THIRD-MONTH RESULTS

A BASED ON SYMPTOMS DURING MENSTRUAL PHASE ONLY

Pre treatment category	Treated					Controls					% improved one or more categories		% improved two or more categories	
	3rd month classification					3rd month classification								
	0	X	2X	3X	Total	0	X	2X	3X	Total	Treated	Controls	Treated	Controls
0														
X	1				1						100			
2X	6	4	5		15	1	3	9		13	67	31	40	8
3X	9	7	2	4	22	2	2	2	16	22	82	27	73	18
	16	11	7	4	38	3	5	11	16	35				

B BASED ON SYMPTOMS DURING PREMENSTRUAL PHASE ONLY

	0	X	2X	3X	Total	0	X	2X	3X	Total	Treated	Controls	Treated	Controls
0	27				27	21				21				
X														
2X	2	1	1		4		2	3		5	75	40	50	
3X	2	5			7	1	1		7	9	100	22	100	22
	31	6	1		38	22	3	3	7	35				

C BASED ON SYMPTOMS DURING PREMENSTRUAL AND MENSTRUAL PHASE COMBINED

	0	X	2X	3X	4X	Total	0	X	2X	3X	4X	5X	6X	Total	Treated	Controls	Treated	Controls
0																		
X	1					1									100			
2X	4	3	4			11	1	1	6					8	64	25	36	12
3X	6	3	2	4		15	1	1	2	9				13	73	31	60	15
4X	2		1		1	4			2		3			5	75	40	75	40
5X																		
6X	2	1	4			7	1		1				7	9	100	22	100	22
	15	7	11	4	1	38	3	2	11	9	3		7	35				

A and B O free from pain X discomfort, 2X pain but no disability 3X incapacity requiring rest in bed
C Summation of Xs in menstrual and premenstrual phases, maximum possible pain 6X (see text)

General Remarks

Vitamin E appeared to have a cumulative effect in most of the successfully treated cases. 20 of the girls who were given vitamin E became entirely free from pain in the premenstrual and menstrual phases This result was obtained in 8 of them in the first month of treatment, but for the remaining 12 the rate of improvement was more gradual—in some cases with relapses in the second month At the end of the course 17 of the treated girls complained only of discomfort during the premenstrual and/or menstrual phases and immediate improvement in the first month had taken place in only 4 of these

At the routine examination a year later some girls who had taken part in the experiment and had received vitamin E tablets said that their pain had recurred It was less severe but had recurred two to six months after treatment These girls asked for a further supply of vitamin E tablets because they had been impressed by the relief given them

Conclusion

The results obtained with vitamin E in the treatment of spasmodic dysmenorrhœa in this controlled investigation appear to be sufficiently encouraging to warrant extended clinical trials

We are indebted to Prof Ralph Picken, the provost of the Welsh National School of Medicine for permission to undertake this test to Dr E Lewis Faning for the statistical analysis and advice; and to Prof A S Duncan for criticism and help in the preparation of the paper We must also thank the wardens of the halls of residence of the University of Wales for their coöperation and Messrs. Roche Products for the vitamin E and placebo tablets

REFERENCES

Adamstone, F B (1931) *J Morph.* 52, 47
Mason, K E (1942) *J Nutr* 23, 59
Shute E. (1942) *J Obstet Gynaec Brit Emp* 49 482

RESIN-IMPREGNATED PLASTERS

Roy H. Maudsley
M B Lpool, F R C S
FORMERLY SENIOR ORTHOPÆDIC REGISTRAR,
ROYAL FREE HOSPITAL, LONDON

Resin mixed with plaster-of paris enables a cast to be applied which is lighter and stronger than the usual one The resin normally used is melamine formaldehyde ('Beetle Resin') which when combined with plaster of paris gives rise to a very hard cast which resists wetting Any delay in the hardening of the resin is avoided by the use of a catalyst such as ammonium chloride which creates the necessary pH for the setting of the resin

At the Royal Free Hospital London resin impregnated plasters have been used for various purposes over the past eighteen months (Maudsley 1954) Records were kept of 100 consecutive plasters of different types the controls were normal plasters of these types The plasters were applied by different members of the staff but the results were sufficiently consistent to draw the following conclusions:

1 A satisfactory resin impregnated plaster-cast requires little more than half the quantity of bandages that a standard plaster requires.

2 The cast is stronger thinner lighter and more durable than the standard plaster It is preferred by the patient who has experienced both types.

3 Very few walking plasters have been cracked or become soft at the heels and the edges have remained firm despite the frequent washing of the adjacent parts

4 Plasters exposed to rain are not impaired and they may be washed if contaminated They are particularly useful in children

5 The economy has been considerable

Until recently the technique depended on dipping normal 'Gypsona' plaster bandages in a freshly prepared solution of resin and catalyst (Morrison 1953) The trouble that this involved was felt to be justified by the increased quality of the cast No serious disadvantages have been encountered a resin plaster of optimum thickness is easy to remove but a thick one may be difficult. In over 300 cases in which such plasters were applied there was only 1 skin reaction this was an exacerbation of psoriasis Should tingling of the hands occur when using resin plaster, this may be stopped by wearing rubber gloves.

We have now had for trial experimental bandages in which the resin and catalyst are incorporated with the plaster during the manufacturing process and which apparently remain stable In a small series of 20 plaster casts the numbers of experimental bandages used were about half the number used in controls with the usual plaster but the two types of resin impregnated casts did not differ in quality While with normal plaster bandages there is an appreciable loss of plaster when the bandages are squeezed after wetting this loss is negligible in the case of the experimental bandages which may be squeezed very firmly after wetting This small plaster loss means that practically the whole plaster content of the bandages is utilised in the construction of the cast mess is reduced and there is little risk of drains being blocked by resin containing plaster-of paris.

It is expected that resin plasters will prove most useful in both fracture clinics and general orthopædic practice.

I am grateful to Messrs. Smith & Nephew Research Hunsdon Hertfordshire for supplies of the experimental bandage

REFERENCES

Maudsley R H (1954) *Lancet* i 106
Morrison, J B (1953) *Ibid* ii 1317

Preliminary Communication

AN APPARENTLY HOMOGENEOUS SUBSTANCE WITH INTRINSIC FACTOR ACTIVITY ASSOCIATED WITH CELL PARTICLES FROM HUMAN STOMACH

The intrinsic factor of Castle is secreted by the mucosa of the fundus of the human stomach into the gastric juice Little however, is known of the form in which intrinsic factor exists within the mucosal cells The following experiments suggest that part of the intrinsic factor activity of human gastric mucosa is associated with cell particles and the particular substance involved has been isolated in an apparently homogeneous state

Each stomach obtained at operation for duodenal ulcer is placed at once in a vessel surrounded by an ice salt water mixture The mucous membrane is removed washed free from surface blood and mucus with isotonic saline at 0–5°C and cut into pieces about 0 5 sq cm area which are extracted with 2% (w/v) NaCl solution in a macerator for 5 minutes The temperature is not allowed to rise above 12°C Debris is removed by centrifugation at 2000 r p m for 20 minutes and the pale red supernatant liquid (A) is stored in the frozen state for up to 2 months until an adequate amount of material has been accumulated

This material is centrifuged in the 'Spinco' ultracentrifuge using the 20 rotor and subjected at maximal speed to approximately 38 000 g for 10 minutes The clear red supernatant (Z) is carefully removed from the precipitate (B) which has three layers the middle one accounting for about 75% of the whole The precipitate (B) is resuspended in ice-cold distilled water stirred intermittently for 10 minutes and recentrifuged for 20 minutes at 2000 r p m The colourless supernatants (C) from this and two further extractions are mixed and

STAGES IN THE PREPARATION OF INTRINSIC FACTOR SUBSTANCE

Stage		% fæcal excretion of radioactivity after 0 5 μg test dose of ^{60}Co vitamin B_{12}	
		^{60}Co-B_{12} without extract	^{60}Co B_{12} with extract
1 Macerated mucous membrane in 2% NaCl	Debris	90	85
	Supernatant A	92	43
2 A, ultracentrifuged	Supernatant Z	86	51
	Precipitate B	86	44
3 B, extracted with water	Precipitate	94	89
	Supernatant C	94	56
4 C, dialysed against water	Flocculent precip	90	94
	Supernatant D	90	58
5 D, concentrated against gum arabic	Flocculent precip	97	94
	Supernatant E	97	65

dialysed at 0–5°C against glass distilled water until free from chloride ions During dialysis a flocculent precipitate develops which is removed by centrifugation and discarded If the supernatant (D), which has intrinsic-factor activity (see table) is now freeze-dried, the resulting very pale yellow powder, dissolved in phosphate buffer of 0 1 M strength at pH 7 9, shows two electrophoretic protein components both on paper and in the Tiselius apparatus Separation of these components may be achieved by concentrating the extract to about one-fifth of its volume by dialysis at 0–5°C against 20% dextran (Benger) or 50% gum-arabic in water A flocculent precipitate develops which may be removed by centrifugation and the pale yellow supernatant (E) is found after equilibration overnight against phosphate buffer of 0 1 M strength and pH 7 9, to contain only one protein component when analysed electrophoretically on paper and in the Tiselius apparatus and ultra centrifugally in the Svedberg ultracentrifuge

Intrinsic-factor activity has been assayed in patients with addisonian pernicious anæmia by measuring the difference of fæcal excretion of radioactivity after an oral dose (0 5 μg) of cobalt 60 labelled vitamin B_{12} given alone and with the extract to be tested The technique has been fully described elsewhere [1] The amount of material used for assay at each stage in the preparation of substance E represents approximately that derived from one-third of a stomach as removed by partial gastrectomy The method of preparation has been repeated in all but its final stage on four occasions and typical assay results for the various steps are set out in the table

Substance E is pale yellow and will promote the absorption of 32% of radioactive B_{12} in a dose of 10 mg Its chemical composition is under investigation and awaits the preparation of several different samples of the material Ultracentrifugal data indicate an approximate molecular weight of 40,000

Microscopic examination of the precipitate B indicates that it consists of a lower layer composed mainly of damaged cells, a middle layer mainly of mitochondria, and an uppermost layer mainly of microsomes The supernatant (Z) contained some microsomes and a few mitochondria engulfed in mucus The method of preparation of substance E would therefore suggest that it is associated in the cell with the nuclei, mitochondria, or microsomes which are precipitated in the ultracentrifuge together with mucoid material It will be observed however that much intrinsic-factor activity remains in the supernatant Z; and it is possible that the activity of precipitate B might be caused not by particle bound intrinsic factor but by adsorption of intrinsic factor from the supernatant on to mucoid material This possibility was tested by re adding the precipitate obtained in stage 3 to the supernatant Z in order to allow further adsorption to take place This, however, did not occur It would seem therefore that intrinsic factor activity may be present in bound form provided that the adsorbing power of the precipitate had not been lost The activity present in supernatant Z awaits further investigation It may be due to a second substance or to activity from disrupted cell particles

The relation of substance E to the intrinsic factor prepared by Latner and his co-workers [2] is obscure Our material is much less active, of higher molecular weight and slightly coloured One possibility is that it may be a precursor of intrinsic factor secreted by the mucosa into the gastric juice

We wish to thank Mr G E Moloney for suggesting the use of, and providing, the material which made this work possible, Mr B Collett for technical assistance, and Dr R E Davies for advice on the microscopical examination of the precipitates

J R P O'BRIEN
B Sc , M A. Oxfd
W H TAYLOR
B M Oxfd, M R C P,
Department of Biochemistry
Radcliffe Infirmary
University of Oxford

A L TURNBULL
D.M Oxfd M R C.P
L J WITTS
D M Oxfd, M D Manc.,
F R C.P
Nuffield Department of Medicine,
Radcliffe Infirmary,
University of Oxford

New Inventions

LEG STIRRUPS FOR CYSTOSCOPY

THE best position for cystoscopy was emphasised by Macalpine [3] in 1936 Since then various types of leg supports have been designed, from the triple jointed St Mark's rests to the simple wide arc stirrups of Page [4]

The hip should not be flexed more than 60°, so that the pelvis remains flat on the table The cystoscope can then be introduced in the male without putting undu tension on the suspensory ligament of the penis Th full lithotomy position is not only inconvenient fo cystoscopy but also carries the risk of straining th intervertebral and sacro iliac joints Schleyer Saunders draws attention to this as a possible cause of postoperativ backache in women after gynæcological operations In old people, who comprise a large proportion of urologica patients, this danger is increased by osteo arthritis and decalcification of the bones As Page [4] points out, the buttocks should rest at the end of the table to allow free movement for the surgeon

The leg stirrups illustrated here have been in use in the urological unit in Bristol for the past two years The legs are held in loose canvas slings with no popliteal compression These slings are fixed to the outer sides of the poles and hook on to the inner sides The sling supports the full length of the calf and prevents excessive abduction of the thighs The poles are insulated with rubber to avoid the chance of burns from diathermy earthing

The poles are fixed to the runners of the table by simple thumb screw clamps which do not have to tightened excessively, because the poles retain th position by friction from the weight of the limb, actin on the clamps through a long leverage If the weig

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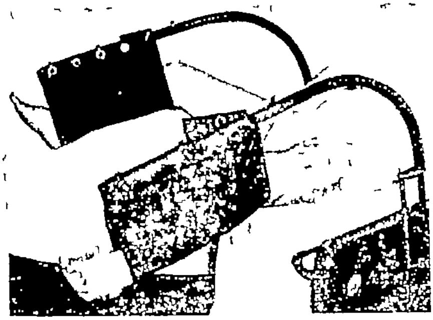
[1] Callender [illegible] Turnbull, A , Wakisaka, G *Brit med J* 1954, [illegible]

[2] Latner A L Merrills R J , Raine L C D P *Lancet*, 19 i 497

[3] Macalpine J B Cystoscopy and Urography Bristol, 193 p 48

[4] Page, B H *Lancet*, 1953 ii, 700

[5] Schleyer Saunders, E *Brit med J* 1954, i, 28



Leg stirrups in position for cystoscopy

of the limb is taken by an assistant, the poles can be readily adjusted into any position to accommodate a patient with a stiff hip or other deformity of the lower limb which may produce a serious problem for the urologist. For the passage of urethral dilators it is often an advantage to have the lower limbs straight this position can be obtained by lowering and adducting both stirrups without having to re towel the patient These poles are easy to manipulate and simple to understand and are not confusing for the most junior nurse, who may be the only available unscrubbed person in the theatre at that moment

Small restrainers are placed on the table end of the poles to prevent complete adduction of the thighs should the anæsthesia happen to be too light

My thanks are due to Mr F Christmas, of the United Bristol Hospitals, for his help in constructing the prototype illustrated here Messrs. C F Thackray Ltd are now manufacturing these stirrups

Bristol

J P MITCHELL
F.R.C.S

A PARALLEL BEAM PORTABLE THEATRE-SPOTLIGHT

THE design of portable theatre-spotlights appears in most cases to have fallen between two stools they are neither true spotlights nor do they give a shadowless light The reflector is usually 15–18 in in diameter bulky, and requires refocusing every time the distance from the lamp to the operating field is altered This distance may vary from 3 ft to 8 ft during an operation but is usually from 3 ft. 6 in to 4 ft 6 in When a lamp of the usual design is focused on an object 4 ft. away a movement of as little as 1 ft. in either direction produces a "ring effect" with falling off of axial illumination Since the diameter of the retracted incision is usually no more than 6 in the wound itself may correspond to the dark centre of the ring" while the edges of the incision may be distractingly bright The diameter of 18 in in the orthodox theatre-spotlight is a futile attempt to provide a source of shadowless illumination The reason for this is clear when one compares the relatively small size of the reflector of the orthodox spotlight with that of the very large main overhead theatre light

Thus there is a need for a high-efficiency parallel beam spotlight for use as an accessory lamp to the main overhead theatre light The need for a lamp of similar specification (though not for the same purpose) was met in the motor industry by the Lucas 700 S L R lamp more commonly known as the Lucas flame thrower, recognised so easily on the road at night by its pencil beam of extraordinary brilliance This lamp (fig 1) has a reflector only 7 in in diameter giving a parallel beam of an intensity far greater than that of any other spotlight with which it has been compared The source of light is a 12 V 48 W prefocused bulb shielded so effectively that there is no glare or dazzle unless one is in the line of the beam Research on whether this lamp could be used as a form of theatre lighting was made in the experimental department of Messrs Lucas, and we found that for theatre purposes a slightly converging beam was even more effective This could easily be obtained by bending the bulb flange so as to allow the bulb to advance forwards along the axis of the reflector

Some heat can be felt in the line of the beam but it is not objectionable and can be reduced if necessary to a minimum by using a heat filter

Although the lamp was primarily designed to work from an accumulator we have for convenience, used a transformer as a source of power thus dropping the voltage to that of an accumulator—i e 12 V Since the source of power is optional, this lamp can provide a form of auxiliary lighting in an emergency

The lamp is mounted on a simple sliding tubular column, whose height can be varied, and a ball and socket joint connects the lamp to an upper and wry necked tube allowing a wide range of movement This is facilitated by a small handle riveted to the lamp housing The lamp base is cruciform, with conducting rubber wheels and has a transformer recessed within it (fig 2)

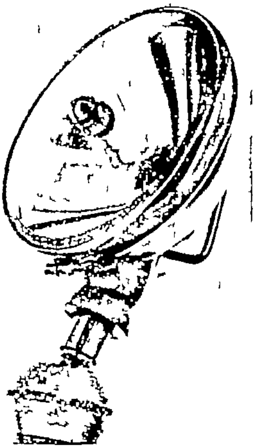


Fig 1

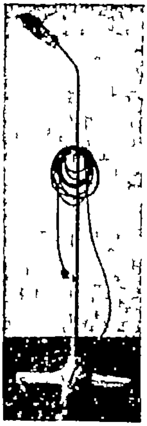


Fig 2.

The lamp has been of great use in gall bladder pelvic, and perineal surgery The beam is so powerful that it can be reflected from retractor blades thus illuminating the depths of the wound This lamp is obviously not the complete answer to the problem of the second theatre light' but it throws a powerful beam which can accurately and easily be directed without the need for refocusing; moreover it is inexpensive

I wish to thank Mr Arnold Gourovitch, F R.C.S.; the staff of the experimental department of Lucas Ltd for help in the design of this lamp Mr F Bradshaw and Mr W Smith for its construction and Mr T Dee clinical photographer for the illustrations.

The Queen Elizabeth Hospital,
Birmingham

P DAWSON EDWARDS
F.R.C.S.

Reviews of Books

Reflections on Renal Function

James R Robinson, M D, PH D Camb, assistant director of research, department of experimental medicine, Medical Research Council and University of Cambridge Oxford Blackwell Scientific Publications 1954 Pp 163 17s 6d

In his discourse on the working of the kidneys Dr Robinson achieves exactly what he set out to do He presents, in moderate compass, "a clear picture without concealing its incompleteness and lack of finality" Lucidity is the outstanding virtue of this short book which surveys a great deal of ground tersely but unhurriedly These "reflections" make interesting reading because the recalcitrant problems of renal physiology are contemplated from several viewpoints, because controversial findings are described *sine ira et studio*, and because Dr Robinson's thinking is vigorous, and firmly tethered to experimental evidence, straying neither into dogma nor speculation The distribution of emphasis is uneven, which reflects partly the patchiness of present knowledge, partly the author's special interests

The treatise begins with a brief but excellent critical discussion of the concept of clearance and its application to the measurement of glomerular filtration This is followed by a short account of tubular reabsorptive processes Tubular secretion, for the sake of its theoretical aspects, is considered at length *The chapters dealing with the excretion of sodium* and water, the tonicity of the urine, and the allied problem of regulation of the volume of the body fluids, are unconventional and interesting Here—but not in other sections of the book—reasonable familiarity with the basic experimental facts and with the relevant literature is essential to understand the argument By contrast, renal control of acid-base balance is described in more elementary fashion A short, disappointing chapter on the regulation of renal function deals exclusively with limitations of renal function, while much of what is known about the control of renal behaviour is included in the final chapter which appraises the kidneys' unexplained success in conserving the volume of the body fluids

The great value of Dr Robinson's exposition derives from his approach to his subject The "lack of finality" of the picture is made its focal point, and thus becomes a stimulating challenge to further research and further reflection This book will not only serve students reading for an honours degree in physiology, to whom the original lectures were addressed It will help greatly all newcomers to active renal research, and it should be particularly useful to those who have to teach medical students but lack first-hand knowledge of renal physiology and its voluminous literature

Medical History of the Second World War

The Civilian Health and Medical Services Vol II The Colonies, the Medical Services of the Ministry of Pensions, Public Health in Scotland, Public Health in Northern Ireland Editor Sir Arthur MacNalty, K C B, M D, F R C P, F R C S London H.M Stationery Office 1955 Pp 406 45s

This is the 11th volume of the medical history and no less than the 35th of the whole series of official histories of the late war There are 9 more to come in the medical and at least 40 more in the general series Will these war memorials of paper seem to our (problematical) descendants more worthy than the spate of stone and bronze that followed the first world war?

All the sections of this latest volume are of a high quality, but, from the nature of the story, the narratives on Hong-Kong and Malaya are the most exciting—and depressing Sir Selwyn Selwyn-Clarke's Hong-Kong story has a particularly valuable passage on "lessons learnt," and both he and Dr R B MacGregor for Malaya stress the undue effort put into evacuation schemes which failed to be acceptable to the people, and the immense difficulties caused by the lack of any plans or instructions envisaging defeat and the occupation of these Colonies The [illegible] and heroic stories of internment life under [illegible] are full of medical and human interest, though the unanimously low opinion of Japanese intelligence is a wry comment on our own failure to defend Hong-Kong for more than 18 days and Malaya for more than 9 weeks Professor Bernard's account of the splendid resistance of Malta, G C, is a close runner up in interest It is depressing to read of the rise in undulant fever from 1944 when supplies of goats' milk increased and its compulsory pasteurisation was relaxed

Dr A. Sandison's story of the medical side of the work of the Ministry of Pensions is a model of clarity and comprehensiveness, while Scotland has been admirab covered by Sir Andrew Davidson, Dr A K Bowman, a Dr R J Peters, and Northern Ireland by the Minist of Health and Local Government and Dr J Boyd

The Clinical Significance of Disturbances in the Delive of Sweat

Marion B Sulzberger, M D, F A C P department dermatology and syphilology, New York University Po graduate Medical School, Franz Herrmann, M.I skin and cancer unit of University Hospital, New Yo University Springfield Ill Charles C Thom Oxford Blackwell Scientific Publications 1954. P 212 50s

This monograph in the American Lecture Series an expert précis and critical review of what is know about the physiology and pathology of sweating

Part 1 describes methods of investigating insensible a sensible sweating and gives physiological data about regio differences of sweating on the body surface and of the influen of age, sex, and race Part 2 deals with quantitative a qualitative variations, the difference between emotional a thermogenic sweating, and other forms due to toxic su stances, degeneration of nerve tracts, or localised phenomena such as gustatory hyperhidrosis, and axillary hyperhidro on undressing before the doctor Forms of hypohidrosis a anhidrosis include those due to agenesis, defective nerv *mechanisms, degeneration of the glands, or obstruction of t* ductal orifices Dr Sulzberger and Dr Herrmann stret the term "dyshidrosis" to include coloured sweat, bloo *sweat, and offensive sweat, as well as the pompholyx type* eruption to which it was applied by Tilbury Fox in 18 They believe that some instances of pompholyx are, in p at least, related to sweat-duct obstruction, despite rec observations that the ducts veer round and do not p into the vesicles They emphasise that these eruptions a characteristically worse in hot weather and suggest that vicious circle of hyperhidrosis, surface stagnation of swe swelling of keratin, ostial occlusion, sweat retention, and ve culation may account for the clinical features An interesti section attributes diminution of sweating to a decrease electrophysiological potential along the ducts Part 3 discus most adequately the difficult problem of treatment disorders of sweating

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Modern Treatment Yearbook 1955 (21st ed Londo Ballière, Tindall, & Cox [for the *Medical Press*] 1955 P 344 25s)—In 1930, when the first edition of this yearbo for general practitioners appeared, we pointed out that editor must have had difficulty in deciding what informati was needed particularly by general practitioners and not b the rest of the profession In this edition the problem wa probably rather different The general practitioner has lo been something of a specialist in social and preventi medicine, *but no practitioner today is so specialised that h* can afford to ignore the advances in other therapeutic field This volume gives a concise and interesting account of thes advances Each of the 36 articles has been written by a authority, and the book as a whole is a remarkably compl statement of modern therapeutic opinion

Emotions and Bodily Changes (4th ed New York Columbia University Press 1954 Pp 4442 £6)—When she set herself, in 1935, the task of surveying published wor on psychosomatic interrelationships, Dr Flanders Dunbar can hardly have foreseen that she was casting herself f the rôle of sorcerer's apprentice Her pages have multipl in these twenty years from a modest 595 to 4442; and th monumental piece of industry presents both full or partial abstracts of relevant papers, 'selected with a view to orienta tion and focus,' and a superb bibliography for those makin fuller studies It is not only a reference work it is also a stimulating, well written, and amusing guide

THE LANCET
LONDON SATURDAY, APRIL 23, 1955

Poliomyelitis Vaccines

THE results of last year's trial of poliomyelitis vaccine in the United States, under the auspices of the National Foundation for Infantile Paralysis, have now been announced, and first impressions are very favourable The complexities of the trial make it hard to give a comprehensive figure for the efficacy of the vaccine in protecting against paralytic poliomyelitis, but summaries of the evidence [1] suggest that the advantage it gives to vaccinated over non vaccinated children is about $3^1/_2$ to 1 —a remarkably high figure considering how short was the time for overcoming the many technical difficulties in a trial of this kind. As, even in an epidemic, the number of cases of poliomyelitis which declare themselves by developing paralysis is comparatively small, no trial of a protective vaccine will provide satisfactory data unless it includes a great many people In this trial some 400,000 children received three intramuscular injections of vaccine in the course of five weeks and about 200,000 children were given three "dummy" injections. In addition, about 800,000 children of roughly the same age were observed as uninoculated controls The vaccine was prepared by growing a representative strain of all three serological types of poliomyelitis virus in tissue cultures of monkey kidney cells, and the virus was then inactivated by treatment with formaldehyde at 37°C Healthy tuberculin negative rhesus monkeys provided the kidney tissue, and the final material was rigorously tested to ensure that the infectivity of the virus was destroyed and that no micro-organisms pathogenic for man were present Dr J E SALK and his colleagues in Pittsburgh were largely responsible for the technical development of the vaccine, and most of the virus used in the trial was prepared in the Connaught Laboratories Toronto

The results of the trial are given in a report [2] by Dr THOMAS FRANCIS director of the Poliomyelitis Vaccine Evaluation Centre In a population of 1,829,916 children there were 1013 cases of poliomyelitis during the study period of about eight months In the evaluation, the trial was considered in two parts in some areas vaccinated children were compared with children who had had dummy injections and in other areas vaccinated children were compared with uninoculated controls In the first, called 'placebo control' areas there were 33 paralytic cases among about 200 000 children receiving vaccine, compared with 115 cases among about 200 000 "dummy" controls Similarly, in the 'observed control' areas there were 38 paralytic cases among about 200 000 children receiving vaccine and 330 cases among about 800 000 uninoculated children The advantage of vaccinated to control children in terms of paralytic disease thus appears to be about $3^1/_2$ to 1 in the placebo areas and rather better than 2 to 1 in the observed areas. There was wide variation in the response to different batches of vaccine, and in general the protection against viruses of types 2 and 3 was better than that against type 1 This had been expected from the results of antibody measurements —and unhappily type 1 is at present the cause of most cases of paralytic poliomyelitis The most striking effect of the vaccine was in preventing bulbo spinal disease, in which the estimate of effectiveness of the vaccine for the placebo control areas was 94%, with a lower limit of 81% The effect noted in spinal paralytic poliomyelitis was less striking—60% with a lower limit of 30% In observed control areas these differences were less pronounced but still highly significant It seemed that there was a progressive increase in effectiveness with increase in age, as far as could be judged from the limited data and the narrow age span in this trial In the incidence of non paralytic disease there was no significant difference between the vaccinated and control groups, and when these cases and those considered not to be poliomyelitis are removed, leaving only paralytic cases, effectiveness was estimated at 72% in the placebo control areas and 62% in the observed control areas FRANCIS adds that the estimates would be more secure had there been more cases of poliomyelitis.

A disadvantage of this form of vaccination is that the immunity it confers may not last long Data from the bleedings performed five months after inoculation indicate some persistence of antibodies but a decline in antibody titre particularly in children vaccinated with "poor" batches of vaccine, and SALK is reported to have said that children vaccinated last year should be given a booster inoculation this year [3] He has since suggested [4] a change in the timing of the three injections and we understand that the new procedure will be used for primary vaccinations undertaken this year He now believes that the best plan is to separate the first two injections by two to four weeks, and then to wait for at least seven months before giving the third dose The third injection "should then extend the immunity for an indefinite period, perhaps years, and maybe even a lifetime" [4] This is the vital point, and we hope that what seems at the moment to be an unduly optimistic view will in fact be justified by events But if it is found that contrary to SALK's hopes antibody levels cannot be maintained without a succession of booster doses, then a serious problem will arise Will it be necessary to give injections every year, or every few years, and, if so, for how long should they be given? The report on the trial emphasises the safety of the vaccine but if injections are given regularly for several years to millions of children the risk of allergic reactions to monkey kidney tissue will become increasingly grave We do not yet see any reason to be less anxious on this account than we were six months ago [5] Moreover it is not as if there were no alternative even though passive immunisation with gamma globulin has proved disappointing there is still a very good hope that avirulent strains of virus may be used safely and successfully Immunisation with live avirulent poliomyelitis virus should, like natural infection, give life-long immunity, and there are many who believe that live avirulent variants will provide the ideal method of immunisation and that such vaccines may be available before long In a new World Health Organisation monograph[6] both Sabin and Koprowski favour the ultimate answer of live avirulent poliomyelitis virus in preference to inactivated virus, and they have made considerable advances both in preparing avirulent variants from all three antigenic varieties of virus and in testing some of them in man. There are many difficulties ahead in this field, but there is no reason to believe that they cannot be overcome in the next few years The advantages of both forms of vaccination might perhaps be combined by giving live avirulent virus under the temporary protection of immunity conferred by inactive vaccine

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[1] *Manchester Guardian* April 14 1955

[2] See *New York Times* April 13, 1955

[3] *Manchester Guardian* April 13 1955

[4] *New York Times* April 15 1955

[5] *Lancet* 1954 ii, 851

Naturally enough, the ring of news from America has convinced many people in this country that we should use the vaccine in large quantities as soon as possible But, even if adequate supplies were ready at once, we should be very reluctant to see them used until the present evidence has been fortified, especially in the matter of sensitisation The Medical Research Council are making plans to try a limited amount of vaccine this year and to study the response to it. It seems to us far wiser to go thus warily rather than embark on a large immunisation campaign with a vaccine whose repeated use may prove harmful, whatever its immediate potency As Sabin has observed,[6] we should not judge that the work is nearly finished it is only just begun

Treatment of Angina Pectoris

The usual cause of angina pectoris is atherosclerosis of the coronary arteries, although aortic valvular disease or anæmia may be contributing factors No known treatment will modify the underlying pathological condition, but much can be done to relieve symptoms Most cardiologists agree that patients with angina of recent and sudden onset should be treated as though they had had a coronary thrombosis and a pending myocardial infarct The patient should be kept in bed, except for his toilet, for four to six weeks, he should eat a reducing diet if he is overweight (and frequent small light meals if he is not), and he should be given heparin for forty eight to seventy-two hours, followed by ethyl biscoumacetate ('Tromexan') or phenylindanedione ('Dindevan') By these means arterial occlusion may be prevented, and the return of pain when the patient gets up and finally resumes his normal activity may be averted When the angina is of longer standing, the main points in treatment are weight reduction, light meals (with a rest after them), avoidance of exertion (especially on cold windy days), sedation, and a warm bedroom If pain comes on, glyceryl trinitrate (gr $^1/_{200}$–$^1/_{100}$), dissolved under the tongue after chewing the tablet, will usually relieve it, and many patients find that a tablet taken before embarking on some unavoidable exertion prevents the onset of pain But this treatment does not stop the progress of the disease, and electrocardiographic studies have shown repeatedly that the changes in the S–T segment and the T-wave associated with ischæmia of the myocardium may persist or become more evident despite the relief of the pain with glyceryl trinitrate Of the other vasodilators the capsule of amyl nitrite is usually less acceptable to the patient because of the flushing and the pounding headache it induces After a short popularity khellin has not proved to have any great advantage, and more recently a longer-acting vasodilator, pentaerythritol tetranitrate, has been introduced This is given regularly throughout the day and reduces the frequency or severity of attacks in about a quarter or a third of patients[1]

In about 5% of patients these measures fail to control a pain which strikes so frequently or on so slight a provocation as to prove crippling, and it is very hard to know how to help these people Various operations have been devised to improve the blood supply to the myocardium or to cut the pain bearing nerve-fibres from the heart[2] But most physicians are reluctant to recommend such operations in patients with cardiovascular disease, particularly when the benefits are uncertain They prefer something less hazardous and more readily controlled For many years Blumgart and his associates in Boston have advocated measures which, by lowering the metabolic needs of the body, reduce the demands made on the heart At first they carried out total thyroidectomy,[3] but the advent of antithyroid drugs removed the need for an operation, and lately suppression of the thyroid gland with radioactive iodine has proved an even more acceptable treatment Their practice is to give three doses of 10 millicuries of radioactive iodine at weekly intervals, or a single dose of 20 millicuries Thereafter, at intervals of one to two months, further single doses are given until hypothyroidism is evident, as judged by the patient's appearance, the blood cholesterol level, and the metabolic rate Other workers prefer in the first place to make the patient hypothyroid with an antithyroid drug, such as thiouracil or carbimazole ('Neomercazole'), and then, when the response to a lowered metabolism has been assessed and shown to ease symptoms, they proceed to suppress the thyroid gland permanently with radioactive iodine This seems a more logical course and, moreover, it reduces the dose of radio iodine required to abolish thyroid action Symptoms improve as hypothyroidism develops, and benefit is usually apparent in from one to six months after the start of treatment When hypothyroidism is established and the angina partially or totally relieved, sufficient thyroid extract or *l* thyroxine is given to maintain maximum relief from heart-disease and minimum discomfort from myxœdema this is usually achieved at a basal metabolic rate of –20% to –25%. Blumgart and his associates have now reported the results of this treatment in 720 patients with angina unresponsive to other forms of medical treatment[4] About three quarters have had very satisfactory responses, with a considerable decrease in the severity or frequency of the pain, and in some instances sufficient improvement to enable them to return to work The same therapeutic plan has been used successfully in patients with intractable congestive cardiac failure, and much the same proportion of patients have improved. Although the hypercholesterolæmia associated with hypothyroidism might be thought on theoretical grounds to involve a risk of further atheroma in the coronary arteries, there is as yet no evidence of this in patients receiving small doses of thyroid hormone.[5]

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[6] World Health Organisation Monograph Series neva 1955

[1] Weltzman D *Brit med J* 1953 ii 1400
[2] See *Lancet* 1954 i, 249
[3] Blumgart, H L, Levine, S A Berlin D D *Arch intern Med* 1953 51 866
[4] Blumgart H L Freedberg A S Kurland, G S *J Amer med Ass* 1955 157, 1

Annotations

THE PRICE OF THE LANCET

WE have to announce, with regret, an increase in the price of THE LANCET. Almost all the costs of production have risen steeply in recent years and we are faced with further rises in the immediate future. To meet these the annual subscription (at home and abroad) will be raised to £3 3s, and the price of single copies to 1s 6d from July 1. Any reader renewing his subscription after that date will be asked to pay £3 3s except that the charge will be reduced to £1 11s 6d for medical students, for doctors within a year of qualification and for those undertaking National Service in H.M. Forces. The rates for the air mail edition will be £1 1s higher than at present.

When we last raised our subscription—in May 1920—we said that we should be delighted when circumstances permit us to return to former prices. The experience of the past thirty five years has taken the edge off such optimism; but we remain sanguine enough to hope that with additional help from our readers we shall presently be able to give additional value to our journal.

MEDICAL EXAMINATIONS FOR SEAFARERS

A MARITIME convention of the International Labour Organisation, requiring everybody employed on sea going vessels to have medical examinations before being signed on and periodically thereafter will come into force this August. It applies to every sea going vessel whether publicly or privately owned which is engaged in the transport of cargo or passengers for the purpose of trade but not to vessels of less than 200 tons gross register tonnage to wooden vessels of primitive build such as dhows and junks to fishing vessels, or to estuarial craft.

The convention was adopted by the Maritime Session of the International Labour Conference at Seattle in 1946 but was only to come into force when ratified by at least seven of the world's principal maritime countries at least four of which must have a million tons of shipping each. These conditions are said to have been fulfilled with the ratification of the convention by the following countries: Argentina Belgium Bulgaria Canada France Italy Norway, Poland Portugal and Uruguay. According to *Lloyd's Register* (1954) these countries between them had a total of just over 18 million tons out of a world total of 97 million tons in 1953 but they could only just fulfil the condition that at least four of the signatories should have a million tons of shipping each: in 1953 France had nearly 4 million Italy nearly 4 million, Norway nearly 7 million, and Canada nearly 2 million of which about half was used on the Great Lakes. Bulgaria one of the signatories of the convention does not appear in *Lloyd's Register* at all. On the other hand the countries which have not signed include Great Britain and Northern Ireland (nearly 19 million) and the United States (27½ million counting 2½ million on the Great Lakes).

For Britain and the U.S.A. to guarantee that *every* seaman in their great merchant shipping fleets will be examined before being signed on would of course be a more serious undertaking than for nations with smaller shipping interests and there might be even greater difficulty in arranging for the subsequent periodic examinations, details of which are not yet known. Obviously, too, the quality of such examinations and the application of their results in each individual case are important. Whether a man shall continue to work or not cannot be decided properly by following some schedule of signs and symptoms but only by knowing a good deal about the man and the tasks he has to perform. Admittedly this is a counsel of perfection, but it would be particularly hard to follow in the peculiar circumstances of the shipping world where periodic medical examination might be feared by the men because it might deprive them of their job and by the employers because it might deprive them of a useful pair of hands. Behind these practical details lies the need to determine the age long divergence of view as to the nature of the Merchant Navy—as to whether it is a service or an industry. Obviously, certain things (like routine medical examinations) can be *required* of a service more readily than of an *industry*.

These may be some of the reasons why the United Kingdom has not as yet felt able to sign the I.L.O. convention. This is not to say that our Government do not approve the principle: indeed, much that the new convention demands is already being done here extremely well. But it would be hard to give a positive assurance that in our vast shipping industry every single man that ever goes to sea on a vessel of 200 tons register or over will for certain receive a medical examination before signing on and periodically thereafter. Perhaps therefore, the chief value of the convention at this stage is as an instrument of international health education: it is another move in what we some years ago described[1] as the "long and arduous campaign for a healthy Merchant Navy" which has "followed the pattern familiar on land, with its battle of environment, battle of personal hygiene, and battle of medical services."

FLUOROHYDROCORTISONE

HALOGENATION of corticosteroids by attaching bromine chlorine or fluorine to the C9 atom in the steroid ring has produced some interesting compounds which, like stilbœstrol in another field are more potent than the naturally occurring hormone.[2] Fluorohydrocortisone is more active than the other halogenated derivatives of hydrocortisone (compound F)[3] and qualitatively its physiological action is similar to that of hydrocortisone. In very small doses it maintains life in adrenalectomised animals, enhances the deposition of liver glycogen and produces thymic involution eosinopenia retention of sodium and increased urinary excretion of potassium.[3-6] The action of fluorohydrocortisone in man has been studied by Bartter[3] and by Thorn and his colleagues.[7-8] Of particular importance is its effect on sodium metabolism. Given by mouth 0.5 mg of fluorohydrocortisone produced in a patient with Addison's disease the same amount of sodium retention as did 2 mg of deoxycortone acetate given by intramuscular injection and the effect of 200 µg of fluorohydrocortisone and of 200 µg of aldosterone was almost identical although the former had a rather longer action. Because it is cheaper than aldosterone and can be given by mouth (in contrast to deoxycortone) fluorohydrocortisone is likely to prove an advance in the treatment of Addison's disease. A single daily dose of 5–10 mg may rescue a patient from a severe addisonian crisis, and as little as 0 25 mg daily or on alternate days may maintain electrolyte balance thereafter But it can readily induce excessive sodium retention, hypertension, and œdema, so it must be given with care Although some patients may remain well on fluorohydrocortisone alone, just as some patients did on deoxycortone alone, others do not feel as fit as they might unless cortisone is given too Thorn et al [7] found that a daily supplement of 2 5 mg of cortisone was usually required

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[5] Blumgart, H L, Freedberg A S, Kurland G S *Amer J Med* 1953 14 665

[1] *Lancet*, 1943, i, 807

[2] Fried J, Sabo, E F *J Amer chem Soc* 1953 75 2273 *Ibid* 1954 76, 1455

[3] Liddle G W, Pechet M M, Bartter F C *Science* 1954, 120 496

[4] Leathem J H, Wolf R C *Proc Soc exp Biol, N Y* 1954 86 724

[5] Borman A, Singer F M *Fed Proc* 1954 13 185

[6] Borman A, Singer F M, Numerof P *Proc Soc exp Biol, N Y* 1954 86 570

[7] Goldfien A, Laidlaw, J C, Haydar N A, Renold A E, Thorn, G W *New Engl J Med* 1955 252 415

[8] Thorn, G W Laidlaw J C Goldfien, A *In* Ciba Foundation Colloquia on Endocrinology Vol 8: The Human Adrenal Cortex Edited by G E W Wolstenholme and M P Cameron. London, 1955 p 305

[9] See *Lancet* 1954 ii 26

Fluorohydrocortisone is also potent as a suppressor of endogenous corticotrophin secretion Doses of 1–10 mg daily have reduced the urinary 17-ketosteroids to normal in adrenogenital virilism secondary to bilateral adrenal hyperplasia A constant watch must be kept for excessive sodium retention, and if there is evidence of this the patient should have a low sodium diet and extra potassium chloride The anti-inflammatory action of 1 mg of fluorohydrocortisone is similar to that of 20 mg of cortisone or hydrocortisone The intense sodium-retaining effect, however, precludes the use of fluorohydrocortisone in this way, except in the topical treatment of skin diseases Here fluorohydrocortisone ointment has been effective, and it is relatively cheap, because a smaller amount of hormone is needed

SKIN LESIONS IN PERIARTERITIS NODOSA

SKIN lesions are found in about 25% of cases of periarteritis nodosa The best-known manifestation is the subcutaneous nodule, though this is found in only 16% of all cases [10] Ketron and Bernstein [11] doubted whether the diagnosis could always be made histologically from the more superficial erythematous or papular eruptions of periarteritis nodosa, because the vessels involved in these changes were too small to show the distinctive lesions of the disease That it may nevertheless be useful to make a biopsy examination of such lesions is shown by the experience of Bureau and Barrière,[12] who describe a fatal case of periarteritis nodosa with various skin lesions including a "new" manifestation—an apparently superficial circumscribed red scaly eruption resembling tinea, which showed clearer histological evidence of periarteritis than the grosser skin lesions elsewhere

Nodules, as Bureau and Barrière point out, are most commonly found along the course of small arteries, particularly on the legs but also on the wrist, forearm, angle of the jaw, forehead, and neck There may be more superficial papular elements, sometimes with central necrosis, reproducing the appearance of some forms of tuberculides Erythematous macules are common, particularly on the limbs, they may become purpuric or lead to a secondary blister with an appearance resembling erythema multiforme Purpura, which is said to be the most common lesion, may be massive Nearly always it is associated with other skin changes—erythema, nodules, or blisters Occasionally there is dull erythematous or cyanotic reticulation of the skin—so called livedo racemosa Telangiectatic plaques have also been seen Necrosis of the skin may develop either in a way resembling familiar forms of gangrene of the extremities or secondary to blisters which break, leading to the formation of sharply outlined ulcers These may be severe and resemble those in the "phagedenic" ulceration [13] which occasionally accompanies ulcerative colitis The mucosæ of the mouth, nose, and rectum may show papular or nodular lesions, transient blisters, necrotic ulcers, or massive infiltration [14] Nasal infiltration with a tuberculoid granuloma was described by Wegener [15] in patients who died and in whom necropsy revealed widespread visceral lesions of this type and in addition the vascular changes of periarteritis nodosa

It is a long clinical jump to Miescher's [16] benign case in which skin infiltration resembling Bazin's disease showed histological changes interpreted as periarteritis nodosa leading into a tuberculoid process Other workers have reported cases in which skin lesions of the clinical and histological type described in the systemic disease have been found in patients who remained otherwise well Perhaps until the significance of the histological lesion of periarteritis nodosa is understood, such cases should not be grouped with those of the major disease It is not yet clear what types of necrotising arteritis are in fact ætiologically identical, even if their pathogenesis and histological appearance seem similar Bohrod [17] sees enough similarity between them to suggest that they do form a group, whereas Zeek [18] continues to discourage the grouping together of all forms of necrotising arteritis, among which she recognises as many as five categories hypersensitivity arteritis, allergic granulomatous arteritis, rheumatic arteritis, temporal arteritis, and classical periarteritis nodosa

Dermatologists are aware of puzzling cases of skin lesions which have in common two main features—first, histological evidence of vascular inflammation and, secondly, a perplexing lack of evidence of any general physical disease Many of the nodular and necrotising lesions formerly diagnosed as tuberculides are now less confidently regarded as manifestations of tuberculosis Some are called "nodular vasculitis," whereas Gougerot's school impart a more ætiological flavour to their diagnosis of "nodular cutaneous allergides" The evidence for an allergic basis for all of these is unconvincing At present no very useful purpose seems to be served by associating them with periarteritis nodosa in the sense of the classica disease of Kussmaul and Maier

LITHIUM SALTS IN MANIC PSYCHOSIS

THE psychiatric treatment of mania may be difficult and unsatisfactory Sedative drugs often have to b pushed to the point of narcosis or confusion, and even then they may be ineffective Certainly convulsion therapy is usually effective, but the result may be very short-lived and is much less satisfactory than in depressive illness Any new treatment which may be harmless and effective will therefore be sure of an early trial, and lithium salts appear to hold out a limited promise Although they have been used since 1949, following some observations in guineapigs, not many people have been interested in them Schou et al [19] have made a careful clinical assessment of their use in the treatment of 38 cases of mania—30 with the classical "pure" syndrome and 8 with some atypical features, such as delusions and hallucinations Using placebos as a control, they found evidence of sedation in 14 cases and a less definite action in 18, while in 6 there was no effect Improvement appeared to be symptomatic, and patients relapsed soon after lithium was withdrawn The margin between therapeutic and toxic doses was not wide, but with doses of 24–48 m eq of lithium a day no serious intoxication was noted

In practice it is unlikely that this treatment will have more than a limited value, either for temporary effective sedation or for repeated treatment of recurrent mania where the length of the manic phase can reasonably be predicted Nevertheless the mechanism of the metal's action is of considerable interest The timing of the changes that have been observed is important here Lithium has to be given for a week or two to produce its effect though bigger doses act more quickly When it is withdrawn or reduced, judging by minor toxic effects there is an interval of only a few days before a change is seen. This suggests that lithium does not act by displacement of other metal radicals in enzyme systems such as is known to be the case with some other elements The question is certainly worth further study

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[10] Nuzum J W jun, Nuzum J W *Arch intern Med* 1954 94 6

[11] Ketron L W, Bernstein J E *Arch Derm Syph Chicago* 1939 40 929

[12] Bureau Y Barrière H *Ann Derm. Syph Paris* 1954 81 601

[13] Gat [illegible] Vayre J Saint Cyr M *Bull Soc franç Derm* [illegible] 60 313

[14] Civatte J Duperrat B *Ibid*, p 261

[15] Wegener F *Beitr path Anat* 1939 102 36

[16] Miescher G *Dermatologica Basle*, 1946, 92, 225

[17] Bohrod M G Histology of Allergic Lesions *in* Progress in Allergy vol 4 Basle 1954

[18] Zeek P M *New Engl J Med* 1953 248, 764

[19] Schou M, Juel Nielsen N Strömgren, E Voldby, H *J Neurol Psychiat* 1954 17 250

TUBERCULOSIS AND PERSONALITY

EVERY disease has its drawbacks, but most have some advantages, too, which a patient consciously or unconsciously, may choose to exploit Anyone developing pulmonary tuberculosis is almost automatically withdrawn from the hurly burly for a few months and this may be an emotional as well as a physical relief Indeed George Day[1] has suggested that some people succumb to the tubercle bacillus so as to escape from an unbearable situation while others refuse to heal until time produces some beneficial change in the environment to which they must return These are extreme cases but they serve to remind us that a patient when he brings his soma into the sanatorium does not leave his psyche in the hall with his umbrella His personality, in fact is bound to influence his disease quite as much as his disease influences his personality—perhaps on the whole more

Some cases reported by Wittkower Durost, and Laing[2] illustrate this well Of 80 patients with pulmonary tuberculosis, 40 had a favourable course (group A) and 40 an unfavourable course (group B) The groups were well matched as to age, sex and marital and social status, but the average duration of the illness at the time of examination was longer in group B (10·6 years) than in group A (6·4 years) and the average stay in hospital had also been longer (72·7 months for group B compared with 32·2 months for group A) Diagnosis had been early in 20 of group A but only 17 of group B In 5 patients (2 in group A and 3 in group B) the doctor had failed to recognise the illness early but in 14 of group B and 5 of group A delay was due to conscious or unconscious denial of the symptoms This denial may be self-deceiving and cheerful (manic) or defiant and pig headed

Conscious and obstinate refusal was seen in a foreman who said I had a family of young children. I just couldn t see stopping work and in the mother of five children who refused to go into hospital for two years after diagnosis "I said right off I was not going The only way they got me to come was to tell me I was dangerous to the children Unconscious denial was expressed by a young housewife "I caught a cold I spit some blood In our family when we have a little trouble we do not complain When the doctor told me I had tuberculosis I was surprised Tuberculosis! Gee! Me—tuberculosis!

4 of group B and 1 of group A refused major surgical measures the refusals being based on conscious or unconscious fear of mutilation or disfigurement Again 7 of group B and 2 of group A failed to follow the hospital treatment regulations and 17 of group B as compared with 5 of group A interrupted treatment by discharging themselves. Those who took this line were commonly rebellious duty bound and family bound persons Similarly, 10 of group B and 5 of group A failed to follow medical advice after leaving hospital; either they returned prematurely to strenuous sports and pleasures or to heavy work with long hours.

There was no uniform personality type the observers found, among those who failed to do well but an emotional conflict commonly seen among them was between the need to be loved and cared for and the need to express aggression—the usual conflict, in fact of the immature or infantile personality It was expressed in various ways Thus some patients were frankly dependent openly seeking care and protection others concealed this need behind a hostile front, others suppressed their wish for care and sublimated their aggression in an active striving for independence, others repressed their aggression turning it upon themselves as compulsive self driving behaviour On the whole the patients who acknowledged and enjoyed their dependence did well, whereas those who concealed it behind hostility did badly: as the authors put it (thinking in terms of infantile feeding behaviour) suckers' did better than ' biters. Rebelliousness also presaged an unfavourable course unable to form close relationships because of their hostility these patients suffered continuous frustration of their need for care and love Those who had suppressed this need, and sublimated their aggression in constructive and independent activity tended to do well unless their illness had brought their families into want or privation when harassed by guilt and anxiety they were apt to over-exert themselves too soon Patients who had turned their aggression inwards upon themselves were also likely to do badly, perhaps because of an unconscious wish for self punishment

Group A patients on the whole were more mature in personality, suffering less conflict over dependence less concerned about getting attention, and more capable of accepting responsibility Rorschach tests suggested that there were more flexible people in group A and more rigid people—that is, people less capable of adapting to adverse circumstances—in group B 'Flexibility permits the patient to find substitute gratifications for those which had to be abandoned as a result of illness and its treatment, and thus reduces the total amount of his frustration, aggression and resentment, factors that tend to affect the course of treatment in an unfavourable way '—and indeed, the course of life generally The fox who found the grapes were out of reach called them sour—which is usually interpreted as a sign of his envy and jealousy Actually it was a highly mature response as far as he was concerned they *were* sour—that is no longer desirable. He put the thought of them behind him and went off to look for something else to eat A little of this sour grapes philosophy is essential to flexible living

THE BUDGET

ON Tuesday Mr R A Butler said that our problem in this country is how to maintain our material and social progress and also keep in balance with the rest of the world The burden of taxation is far too great, and industry requires a further incentive But the need is for saving rather than spending Because it would encourage personal expenditure, he is not reducing indirect taxation—except for the purchase tax on textiles. On the other hand, some 2 400 000 people will be freed from income-tax by small increases in the allowances before tax is paid; the standard rate goes down by 6*d* in the £, and the lower rates by 3*d* and children s allowances rise from £85 to £100 Many will believe that different concessions would have been socially preferable But the nature of income tax and of its payers is such that, when it is lowered a little only the most conscientious in the ranks of Tuscany can quite forbear to cheer

Prof G W PICKERING has been appointed regius professor of medicine in the University of Oxford.

WE have to record the death on April 10 of Mr ROBERT DAVIES COLLEY C.M.G consulting surgeon to Guy s Hospital A memorial service will be held in the hospital chapel on Wednesday April 27 at 1 45 P.M

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[1] *Lancet* 1946, ii, 763 *Ibid* 1951 i, 1025

[2] Wittkower, E D Durost, H B., Laing W A R *Amer Rev Tuberc* 1955 71 201 290

Special Articles

LEPROSY IN BRITAIN

W H JOPLING
M R C P, M R C P E, D T M & H

SENIOR REGISTRAR, HOSPITAL FOR TROPICAL DISEASES, LONDON, AND THE JORDAN HOSPITAL, EARLSWOOD, SURREY

THOUGH leprosy is still endemic in many countries of Europe, particularly in the south, it fortunately died out in Britain by the end of the 18th century After the second world war, however, there was an influx of cases from abroad, consisting principally of Anglo Indians (Eurasians) who left India after the granting of Independence in 1947, and also of returned soldiers and the wives they had married while overseas To meet the problem presented by these patients, and to minimise the chances of leprosy becoming again endemic in Britain, the Public Health (Leprosy) Regulations [1] were brought into operation in England and Wales on June 22, 1951, making it compulsory for cases of leprosy to be notified direct to the Chief Medical Officer of the Ministry of Health At the same time the disease became notifiable in Scotland, but the Department of Health there instructed that notifications should go through the local medical officers of health To date 175 cases have been notified in Britain, all having acquired their infection overseas Also in 1951, the Ministry of Health appointed an adviser in leprosy (Dr R G Cochrane) and was instrumental in establishing a special hospital for inpatient treatment—namely, the Jordan Hospital, Earlswood, Surrey, administered by University College Hospital and staffed by the Hospital for Tropical Diseases

THE JORDAN HOSPITAL

The hospital was opened in September, 1951, and can accommodate 18 patients in two single storey buildings, one for men and the other for women Each building contains a series of centrally heated flats consisting of a bed-sitting-room, kitchen, bathroom, and lavatory A few of the flats have two bed-sitting-rooms, the two occupants sharing the other facilities, and a new block is now being built to take 6 more patients and to provide more rooms for clinical and laboratory work Seven nationalities are represented among the present patients Anglo-Indians (10), English (2), Cypriots (2) Maltese (1), Latvian (1), Indian (1), African (1) As they all suffer from lepromatous leprosy, the form of the disease which is most infective and most difficult to cure, full use is made of the hospital's facilities for scientific treatment and for research The hospital does not admit non-infective patients requiring treatment for deformities and other late effects of the disease

Occupational Facilities

Keeping the patients occupied is a major problem A system of payments has had to be introduced to encourage regular work in the hospital grounds, and those who make rugs, woollen goods, baskets, and so on, are helped by the occupational therapist and the matron to sell them once the articles have been sterilised Several of the younger patients take correspondence courses There is a recreational block, with television and table tennis, where plays and concerts are produced, and the outdoor tennis court is very popular in summer

Investigations

Regular visits are paid by the consultant physicians (Sir Neil Hamilton Fairley, Sir George McRobert, and Prof A W Woodruff) and by our ophthalmic surgeon, Mr D P Choyce One of my duties is to carry out a skin biopsy and 8 smears on each patient every two months The fact that these tests are made by one person, and the results interpreted by one pathologist, Dr D S Ridley, helps to ensure the uniformity essential in testing new drugs Hæmatological and biochemical investigations are regularly undertaken to detect adverse side effects on blood, marrow, liver, or kidneys

Treatment

Inability to cultivate the human leprosy bacillus in vitro, or to find a susceptible laboratory animal, has led to treatment with tuberculostatic drugs Since 1941 the sulphones have held pride of place, but they are slow in action and there are risks in their use Lowe's [2] long term assessment of sulphone therapy in Eastern Nigeria is favourable, but he acknowledges that reports from elsewhere are less encouraging At the Jordan Hospital the lepromatous patients have responded poorly to various forms of sulphones Although they have shown definite clinical improvement, especially during the first two or three years, bacteriological improvement has been negligible within that time only after four or five years have the bacilli in the skin shown a significant decline in numbers At present there are 10 patients in the hospital who have had three or more years' treatment, mainly with sulphones, yet none has yet had negative skin smears The periods under treatment are $7^1/_2$, $6^1/_2$, $5^3/_4$, $5^1/_2$, 5, $4^1/_2$, $4^1/_4$, $3\,^3/_4$, 3, and 3 years

Many have had bouts of erythema nodosum leprosum, sometimes with enormous numbers of painful transient erythematous nodes high fever, neuritis, insomnia, and depression Such episodes may continue for weeks or months, even if sulphone is immediately stopped, and require skilful management Corticotrophin and cortisone have a dramatic effect on the symptoms, but do not terminate an attack, and in view of the risk of aggravating the underlying disease they should be used only when absolutely necessary and when sulphone is given concurrently The longest period on corticotrophin or cortisone for any one patient at this hospital has been $13^1/_2$ months (three courses of $4^1/_2$ months)

In some patients the brunt of the reaction is borne by peripheral nerves, and pain and tenderness necessitate reduction or stoppage of sulphone until the neuritis subsides If muscle function is threatened, an operation must be undertaken to strip the nerve sheath from the swollen portion of nerve Two patients are particularly subject to swelling and tenderness in one or both median nerves at the wrists, causing the symptoms of the carpal tunnel syndrome [3]—paroxysmal tingling and burning pain in the palms and first three fingers, occurring chiefly at night Leprosy has not previously been recorded as a cause of this syndrome In one of these patients one hand is so severely affected that the median nerve is to be decompressed at the wrist

In two patients the principal complaint during erythema nodosum reactions is arthralgia affecting the knees, and another has iridocyclitis Borderline (dimorphous) cases are particularly liable to the sudden development of a reactional phase with fever, œdema redness and swelling of all skin lesions, neuritis, and rapid increase in bacilli as judged by skin smears One ex patient had such a lepra reaction three to four weeks after beginning sulphone therapy, and was desperately ill for six weeks, by the end of which time he was emaciated and weak, and had severe wasting of the intrinsic muscles of his hands together with bilateral dropped foot

Isoniazid has been given a trial, alone [4] and with sulphone,[5] but has proved disappointing Thiacetazone (TB1) has been found to have some value but is less active than sulphone and is reserved for patients who cannot tolerate the latter Thiacetazone in combination with isoniazid has not given better results than by itself Two other drugs tried are 'Ethizone' (TB3)[6] and diisoamyloxythiocarbanilide

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[1] Lancet 1951, i, 1366 Brit med J 1951, i 1439

[2] Lowe J Lancet 1954, ii 1065

[3] Kremer M, Gilliatt R W Golding J S R Wilson T G *Ibid* 1953 ii 590

[4] Jopling W H Ridley D S *Trans R Soc trop Med Hyg* 1954 48 132

[5] Jopling W H Ridley, D S *To be published*

Care of Hands and Feet

As most of the patients have some degree of peripheral nerve damage, minor injuries are slow to heal and are liable to lead to trophic ulceration New shoes are dangerous unless they are made to measure by an expert Analgesia of the hands makes it difficult to guard against burns especially when cooking and hot-water bottles have had to be strictly forbidden because they are liable to burn the feet or legs If peripheral nerve damage has advanced sufficiently to cause weakness of the muscles of hands or feet, daily physiotherapy is necessary to prevent contractures. Paralysed muscles call for tendon transplantations

Intercurrent Diseases

Though the number of beds is small a wide variety of intercurrent disorders have had to be treated during the three and a half years of the hospital's existence

Surgical operations (performed by Mr H R I Wolfe at the Hospital for Tropical Diseases or by the surgeons at University College Hospital) have included bilateral oöphorectomy for chocolate cysts, osteotomy of the femur for chronic arthritis of the hip lobectomy for bronchial carcinoma hæmorrhoidectomy radical antrostomy and extensive skin grafting for severe burns contracted before admission Medical problems have included paranoid schizophrenia hysteria, diabetes mellitus idiopathic epilepsy renal amyloidosis pyelitis and various helminthic diseases and acute infections.

PERSONAL PROBLEMS

Perhaps in no other disease is the doctor patient relationship so important as it is in leprosy for not only is progress slow and treatment prolonged but the sufferer is liable to periods of frustration and despair and to periods of prolonged physical suffering The patients who despair have to be given courage to go on those who are worried by domestic or other difficulties need advice; those who quarrel have to be reconciled to each other; those who break regulations have to be gently yet firmly reproved those who are in pain need relief—and this is especially difficult in a long standing disease like leprosy because the best analgesics are habit forming and therefore must be avoided if possible For severe nerve pain I have found small intraneural injections of procaine valuable All these troubles make great demands on the nurses and call for much patience and understanding on their part

The regulations regarding notification differ from those in South Africa and Australia in that they contain no statutory powers whereby a patient can be removed to or detained in hospital against his will This means that our patients can discharge themselves from hospital when they so desire and much time has to be spent persuading those who want to leave hospital that it is to their advantage (and to that of their families) to remain as long as their disease is active Not only may dangerous ophthalmic or neuritic reactions appear suddenly and cause permanent damage if not reported early or if not handled expertly but in spite of warnings patients living at home repeatedly burn their hands or injure their feet Mothers of young children find separation hard to tolerate but have to be persuaded to remain in hospital for their children's sake An additional reason for such a patient not returning home before she is cured is the fact that pregnancy must be avoided at all costs not only does it seriously aggravate the disease but it involves all the emotional strain of having the baby sent away immediately after birth Finally experience in handling outpatients has shown that some fail to report regularly for examination and laboratory tests and a few cannot even be relied upon to carry out treatment In an extreme case the patient deliberately discontinued treatment for six years, with disastrous results to herself[7] Fortunately such an occurrence is less likely now that leprosy is notifiable and the Ministry's adviser keeps the notified cases together with their families under review

THE OUTLOOK

Until such time as research workers discover how to cultivate the leprosy bacillus either in vitro or in vivo the clinician must make use of drugs which have a tuberculostatic activity or he may turn to the pathologist for guidance as to how immunity manifests itself in leprosy and as to how the body's defence mechanism can be stimulated so that the macrophage cells no longer protect the bacilli which multiply within them Research workers in many parts of the world are opening up new avenues of thought and endeavour—Hanks and Gray[8] with their work on the rat leprosy bacillus Suter[9] with his studies on the intracellular parasitism of tubercle bacilli Campos[10] with his work on B.C.G vaccination in the prophylaxis of leprosy Lowe and McNulty[11] with their observations on immunology Ridley[12] with his investigations on the significance of antibody, and others too numerous to name

The Jordan Hospital because it can combine detailed clinical observation with the fullest possible pathological control, is in an unrivalled position to develop and perfect new methods of treating this challenging disease

I would like to thank Sir Neil Hamilton Fairley Sir George McRobert and Prof A. W Woodruff for permission to publish details of some of their patients.

POLIOMYELITIS VACCINE

MEDICAL RESEARCH COUNCIL PLANS

THE Medical Research Council have announced that a limited amount of poliomyelitis vaccine of the kind used in the United States will be available to them this year Sufficient will be allocated for the vaccination of small groups of children in a few centres in Great Britain and Northern Ireland in which there are laboratories studying the poliomyelitis virus The arrangements will be made locally The response to the vaccine will be judged serologically and compared with other information obtained from laboratory tests This course the council add is necessary for planning the most effective use of the larger quantities of vaccine which are likely to become available in this country in 1956 They emphasise that the vaccine is at present available only for these limited purposes and that applications for inoculation cannot be entertained

SUPPLIES IN THE UNITED STATES

It is expected that there will not be enough vaccine to meet the first big demands in the United States, but by the end of the summer supplies will probably be adequate[13] President Eisenhower has directed his Secretary of Health Education, and Welfare to organise a voluntary system of allocating the vaccine It has been suggested that Congress should take steps to prevent a black market in the vaccine The manufacturers have undertaken to supply the National Foundation for Infantile Paralysis with sufficient vaccine to immunise all school-children in the first and second grades throughout the United States and its territories A booster dose will be offered to the 500,000 children vaccinated in last year's trial

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[6] Jopling, W. H. Kirwan, L. W. O G *Trans R Soc trop Med Hyg* 19 2 46 656

[7] *Brit. med J* 1953 i 1033.

[8] Hanks J H., Gray, C. T *Int J Leprosy* 1954 22, 147

[9] Suter E. *Ibid* 1954 22, 1

[10] Campos N. de S *Ibid* 1953 21 307

[11] Lowe J McNulty F *Brit med J* 1953 ii 579

[12] Ridley, D S *Trans R Soc trop Med Hyg* 1954 48, 400

[13] *New York Times* April 14 1955

REACTIONS IN OTHER COUNTRIES

Dr Herdis von Magnus, of the State Serum Institute in Copenhagen, is reported[14] as saying she had heard from Dr Salk that the results of further investigations were even more favourable than those already published She found it difficult to understand objections raised in Britain, France, and Norway that the vaccine would not be as successful in Europe as in the United States In Geneva Dr A M Payne, of the World Health Organisation's division of communicable diseases, pointed to the as yet little known properties of the vaccine, and said he thought that poliomyelitis was not yet beaten In Paris, the French Minister of Health said that France would mass-produce a similar vaccine developed by Prof Pierre Lepine[15] The Swedish board of medicine have ordered enough American vaccine for 100,000 people A Swedish vaccine, using human and not monkey tissue, will also be given

A COURSE IN FAMILY PSYCHIATRY

PSYCHOSIS is found in about 0 5% of the population, mental deficiency in about 1% What fraction these conditions represent of the total mental illness in the country is hard to estimate, but neuroses of varying degrees of severity are so common that it cannot be a large one Patients with psychosis and mental defect fill nearly half our hospital beds, and in industry neurosis is responsible for about a third of all absences from work due to illness[16]

It is now generally held that the public health service should begin to develop a formal mental-health programme[17], and there are signs of a growing interest in this subject among school medical officers This was illustrated at a refresher course in child psychiatry arranged by Dr J G Howells, and held at the end of March by the child psychiatry department of the Ipswich group hospitals In this, the second year of the course, those taking it included 13 school medical officers, 9 general practitioners, 3 psychiatrists, and 2 pædiatricians The general practitioners came mostly from the area of the East Anglian Regional Hospital Board, but the school doctors came from all parts of the country, including Scotland. Last year only 16 people attended the entire course, and 10 came for parts of it, this year 27 members were attending full-time, and only 2 or 3 part-time The growth of interest among general practitioners in the psychiatry of childhood is shown by the fact that in 1947 only 3% of the children attending the department's clinic were referred by their family doctors now nearly 70% of them are referred from this source Dr Howells estimates that if about 5 general practitioners attend the course every year, by the end of ten years most of the partnerships in the area will have been represented (More still would attend, he thinks, if they were able to claim expenses for putting in a locum during their absence, but at present the Ministry of Health is not willing to meet this expense for doctors attending courses arranged by "other persons" than universities and medical schools, although the 1946 Act permits such payments to be made)

The course lasts four days, the first three sessions being concerned with the three main reactions—neurotic, delinquent, and psychosomatic—of children to emotional stress The fourth session dealt with adolescent reactions, and in a fifth session all these subjects were brought together in a consideration of the family as a whole. The last three sessions covered speech difficulties, epilepsy, and the emotional aspects of mental deficiency, cerebral palsy, and psychosis At these sessions, Dr Howells, as tutor, demonstrated a long case, and after a pause for questions and discussion, summed up He then showed short cases relative to the same general theme, and again allowed a short period for questions These lecture sessions alternated with demonstrations, conducted by members of the psychiatric team of the department, on psychometry, play therapy, bibliotherapy, and record-keeping

"Bibliotherapy" in this context means the use of reading matter for therapeutic purposes, and books and papers used in this way were shown at the demonstration The department lends parents articles and books on childhood problems, and also keeps a small lending library of children's books. At the end of the play session each child can borrow a book, which he brings back to exchange for another at the next session The stories help to keep the child in touch with the clinic between sessions and make good topics of conversation All members of the course had been supplied with a list of books recommended for their own reading, and these too were shown at the demonstration

Finally, a demonstration had been arranged, at one of the hospitals of the group, of the electro encephalographic examination of a child Attendance at demonstrations was kept small and wieldy by splitting the members of the course into four groups, and repeating the demonstrations for each group in turn From the interest taken and the questions asked it was clear that the course was proving useful even to those already engaged in psychiatry The lectures were well founded in experimental work, and the point was repeatedly made that the child cannot be treated apart from his family as Dr Howells put it, "the neurotic reaction of the child is a reaction to an emotional battering from the neurotic or disturbed adult"

This seems at present to be the only course of its kind in the country

Medicine and the Law

Bogus Doctor Fined

A FORMER medical student has been fined £100 for forging a letter purporting to show that he was a qualified doctor[1]

Reginald Morgan Ford, aged 35, pleaded guilty to forging a letter from the chief clerk of the General Medical Council purporting to show that he was a graduate in medicine and surgery of the University of Bristol, held the degrees of M B and CH B, and was registered in the Medical Register

Ford had been accepted as an assistant and subsequently produced the forged letter to support his claim to be a doctor He never purchased dangerous drugs He had entered Bristol University in 1947 but was later expelled for a breach of discipline On Ford's behalf it was stated that he had offered to repay money paid for his services while posing as a doctor but the principal had declined the offer because he was satisfied with his work whether practised under deception or otherwise

The Recorder, in passing sentence, said that until he heard the mitigating circumstances he had thought it would be a case for a prison sentence, but he felt after hearing them that no good purpose would be done by sending him to prison "There is no doubt," the Recorder told Ford, "that you were in possession of sufficient skill to satisfy those who became your patients and you appear to have been very careful not in any way to abuse the professional position you wrongly assumed. Apart from being a bad example you have really done no harm"

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[14] Scotsman April 14, 1955

[15] Newcastle Journal April 13, 1955

[16] The Incidence of Neurosis among Factory Workers Medical Research Council Industrial Health Research Board report no 90 London H M Stationery Office 1947 See *Lancet* 1947, ii 254

[17] Jan 15, 1955 p 135 *Ibid* April 2 1955 p 716

[1] *Western Daily Press*, April 5 1955 *Birmingham Post* April 1955

Conferences and Congresses

SYMPOSIUM ON LIVER DISEASES

A SYMPOSIUM on Modern Aspects of Liver and Biliary Disease was held on March 28–April 1 at the Postgraduate Medical School of London The meeting was planned by Dr SHEILA SHERLOCK who arranged a comprehensive course of lectures, demonstrations, and discussions of subjects with practical applications in general medicine and surgery Dr CHARLES NEWMAN dean of the postgraduate school, welcomed more than 60 participants including Dr J CAROLI and Dr V SCHWARTZMANN from Paris, Dr S MADSEN from Copenhagen Dr G A MARTINI from Hamburg and Dr R MANGOLD from Lausanne

Jaundice

The first day s programme concerned problems associated with jaundice and Prof E J KING acted as chairman

Prof N F MACLAGAN reviewed the range of liver function tests and pointed out that certain tests might be positive in diseases which were not primarily hepatic including heart-failure chronic rheumatism malaria and glandular fever A poor prognosis was associated with serum albumin levels of less than 2 g per 100 ml in medical cases and the failure of an increased prothrombin time to respond to vitamin K injections was an unfavourable sign in obstructive jaundice For routine use he recommended examination of the urine for bilirubin bile salts and urobilinogen estimations of serum bilirubin and alkaline phosphatase levels and thymol flocculation and colloidal gold tests Measurement of serum proteins and bromsulphalein retention should be added if indicated

Dr Sherlock classified jaundice and discussed its clinical management She stressed the significance of pain and pruritus in the history and the finer points which might emerge from a thorough physical examination. In the treatment of acute hepatitis she considered that diet should be dictated by the patient's appetite and that the inclinations of the patient should be taken into account in the early stages of mobilisation In chronic obstructive jaundice methyl testosterone for pruritus, fat-soluble vitamins by injection and calcium tablets were of value

Dr F O MACCALLUM said that the lack of a susceptible animal host hindered studies of virus hepatitis Virus A causing infective hepatitis was present in blood and fæces but a carrier state had not been proven Serum hepatitis was caused by virus B which had only been isolated from blood and a carrier state of uncertain duration had been demonstrated Gamma globulin might be given to contacts of infective hepatitis but was of dubious value in serum hepatitis. The two viruses were immunologically different

The significance of positive flocculation tests as an isolated finding after hepatitis was discussed and it was agreed that a careful follow up was indicated but no active measures need be taken Blood-donors should be rejected if they had had an attack of hepatitis Carriers may not have had overt hepatitis and the duration of the carrier state was unknown

On the question of cholangiolitic hepatitis Dr Sherlock remained unconvinced

Dr Caroli pleaded for the wider use of peritoneoscopy in the differential diagnosis of jaundice Prof IAN AIRD considered that this technique demanded great experience and admitted that the type of jaundice was often obscure at laparotomy By serial sampling of blood and duodenal contents following an intravenous dose of bromsulphalein Dr Caroli had found that the excretion time was delayed in obstructive jaundice and normal in hepatitis and he advocated this test in cases of doubt

Cirrhosis and Portal Hypertension

Professor Aird was chairman when Dr Sherlock introduced this subject and explained that the term cirrhosis ' should be restricted to conditions in which the lobular architecture was disturbed A similar histological picture resulted from many causes, because of the limited response of the liver to injury while the clinical features were dominated by those of portal hypertension and inadequate liver-cell function

Current views on the pathogenesis of portal hypertension and its clinical consequences (portal collateral circulation, splenomegaly, and hæmatological changes) were ably summarised by Dr P C REYNELL. In 20% of patients with portal hypertension there was no liver disease and the cause was usually an obstructive lesion of the portal vein

The technique of percutaneous transplenic portal venography was demonstrated by Dr Sherlock Dr R E STEINER, and Dr M D TURNER. The application of this investigation to the diagnosis of portal hypertension and its special use in preoperative assessment were discussed Dr W H J SUMMERSKILL and Dr G A MARTIN showed that the pressure in an occluded hepatic vein, measured through a cardiac catheter provided an alternative index of portal pressure and that other information could also be derived from catheterisation of the hepatic veins A normal occluded hepatic vein pressure with evidence of portal hypertension, was found in patients with thrombosis of the portal vein

Prof R MILNES WALKER discussed the management of portal hypertension The danger of severe hæmorrhage was the only indication for major surgery, but poor liver function or an unsatisfactory general condition might preclude operation Surgical treatment should not be considered for the relief of ascites, but this complication did not necessarily contra indicate operation A preliminary portal venogram was a great help and, when practicable an end to-side portacaval anastomosis was the operation of choice Other portal systemic shunts often became occluded and gastric or œsophageal transection although without operative mortality, was often followed by a recurrence of hæmorrhage

During the discussion it was agreed that the incidence of hepatoma in cirrhosis was 5–15% Most speakers were in favour of eliminating alcohol from the diet of all patients with cirrhosis Dr Sherlock considered that ascites was a contra indication to portacaval anastomosis in cirrhosis but Prof H RODGERS preferred to be less dogmatic. Professor Aird thought that improvement after such an operation could often be attributed to the increased collateral circulation which was encouraged.

Radiology of Biliary Tract

With Prof J MCMICHAEL in the chair, Dr D SUTTON spoke on the radiology of the biliary tract He advocated the use of the intravenous contrast medium Biligrafin especially after cholecystectomy in preference to the oral method and he stressed the importance of cholangiography during operations involving the biliary tract Percutaneous trans-hepatic cholangiography in obstructive jaundice was hazardous because of the risk of biliary peritonitis

Dr Caroli pointed out that biligrafin excretion was related to liver function and though radiology should always be attempted serum bilirubin levels of above 3 mg per 100 ml were seldom compatible with a satisfactory picture

Ascites

In a debate on the problem of ascites in liver disease Dr R I S BAYLISS said that the primary defects of lowered plasma albumin concentration and increased portal venous pressure did not alone always explain the accumulation of fluid Additional factors introduced by the movement of sodium and water into the peritoneal cavity were the diminished output of sodium in urine, sweat, and saliva, possibly associated with increased aldosterone secretion and diminished destruction of other adrenocortical steroids Altered posterior pituitary antidiuretic hormone activity and decreased renal blood-flow might also be of significance

As for treatment, Dr A PATON considered that surgical measures designed to reduce portal venous pressure were dangerous, and methods directed at raising colloid osmotic pressure had only a transient effect The best treatment was paracentesis and then a low-sodium diet (less than 22 m eq Na daily), mercurial diuretics, and ammonium chloride Patients with ascites due to temporary impairment of liver function (alcoholic debauches or gastro intestinal hæmorrhage) responded rapidly to correction of the precipitating factors, and ascites was controlled in most other patients by the conservative régime he had outlined Failure may be due to faulty supervision "Active" liver disease and malignant hepatoma were often associated with intractable ascites which resisted treatment and progressed to a terminal dilution hyponatræmia

During the case demonstrations, it was shown that a good response to treatment was often related to an adequate urinary sodium output in the control period and that relaxation of the régime could sometimes be allowed without deterioration

Dr M D MILNE advocated a combination of potassium and ammonium chlorides in the treatment of ascites, for mercurial diuretics often caused loss of potassium, and Dr Bayliss pointed out that altered capillary permeability might be an important factor in the pathogenesis of ascites

Needle Biopsy

At this session Prof L J WITTS was in the chair Dr Sherlock stressed the safety of the procedure (reported mortality 0 17%) and its wide application in the diagnosis of liver disease, pyrexia of unknown origin, miliary granulomata, reticuloses, and amyloidosis Dr C V HARRISON exhibited biopsy specimens taken from patients in whom the clinical findings were equivocal and explained the histological criteria upon which the diagnosis was made

Hepatic Coma

Dr Sherlock described the mental changes and abnormalities of the motor system in hepatic coma A characteristic electro encephalogram might be found, but was not specific Various factors, either affecting liver function adversely or increasing the nitrogenous material in the intestine, might precipitate the disorder She attributed the syndrome to toxic nitrogenous substances from the portal vein (portal-systemic encephalopathy) and advocated conservative treatment based on the withdrawal of protein, the administration of aureomycin (to reduce bacterial activity in the intestines), and maintenance on glucose

Mr A G RIDDELL also thought that a toxic nitrogenous substance in portal blood was responsible for the neurological disturbance and put forward evidence to incriminate ammonia as the cause in animals and in patients with portacaval anastomoses He referred to the arrest of hæmorrhage by œsophageal tamponage Dr Summerskill demonstrated the relationship of the neurological signs to liver function, portal systemic collateral circulation, and dietary nitrogenous substances Although many signs of hepatic coma could be induced by nitrogenous substances and improved on protein withdrawal, he hesitated to ascribe the whole syndrome to this

During the discussion, it was shown that methionine might precipitate the neurological syndrome without alteration in blood ammonia levels and that its adverse effect was retarded by aureomycin Mr Riddell had found glutamic acid helpful in patients with chronic signs and portacaval shunts, but it had little effect in coma due to liver failure It was considered that methionine had no place in the treatment of liver disease

Some Other Subjects

Colonel W R M DREW considered hepatic *amœbiasis and leptospirosis* both of which were of importance in the United Kingdom The liver was involved in 5-10% of patients with intestinal amœbiasis Jaundice was rare and he did not believe "hepatitis" occurred, only abscess formation Radiology was often crucial in diagnosis Chloroquine was the best drug

Dr A E CLAIREAUX classified the features of *neonatal jaundice* as non-obstructive, in which hæmolysis and inability of the liver to deal with products of hæmolysis were of importance, and obstructive In the second category he included the "inspissated bile syndrome" (which might occur in several diseases) and hepatitis, but he agreed that the classification was not rigid The differential diagnosis of congenital obliteration of the bile duct and viral hepatitis was difficult There was a growing awareness of hepatitis, possibly associated with a carrier state in the mother, as a cause of jaundice in the neonatal period

Dealing with the clinical aspects of neonatal jaundice Dr J W GERRARD said prognosis was difficult and biliary obstruction was sometimes compatible with a long course, with xanthomatosis and hypercholesterolæmia He mentioned two interesting dental manifestations—green milk teeth due to deposition of bile in the dentine and enamel hypoplasia due to poor calcification

Jaundice during pregnancy, said Dr Martini, was either jaundice *of* pregnancy, a relatively uncommon occurrence in toxæmia and associated with only slight bilirubinæmia, or jaundice *in* pregnancy This was usually due to viral hepatitis and, contrary to accepted views, was seldom a severe illness, although fœtal mortality and miscarriage were common in the late stages of pregnancy Jaundice due to gall stones might also arise during pregnancy

Dr W R PITNEY, discussing *coagulation defects* in liver disease, explained that capillary function, platelets and plasma coagulation factors may all be affected in liver disease The commonest defect involved the "prothrombin complex" (prothrombin and factors v and VII) and separate assays were often desirable because the Quick one stage prothrombin-time was relatively insensitive to the abnormal prothrombin levels which might occur in all types of liver disease

Dr Caroli showed an excellent film in which perfusion of the gall bladder was used to demonstrate changes in tone of the *sphincter of Oddi* Reflux into the pancreatic duct occurred in response to fatty meals, high perfusion pressures, or atropine Morphine prevented reflux at high perfusion pressures Surgical measures designed to correct "hypertrophy" of the sphincter were therefore useless

Professor McMichael said that slight elevation of serum bilirubin levels was common in *heart failure* and that "cardiac cirrhosis" (with deranged liver function tests) might occur, especially with tricuspid incompetence Jaundice may be severe, and hæmolysis from pulmonary infarcts may be one cause

Dr Sherlock demonstrated cases of *hæmochromatosis* and stressed the family history, the occurrence in males, the alteration in testicular function, and the incidence of cirrhosis and hepatoma She recommended venesection (500 ml weekly) to remove iron from the body, with careful observation of hæmoglobin and plasma rotein values. Testosterone implants and insulin were aluable supplements

Dr Milne discussing *hepatolenticular degeneration* ointed out that this condition could be distinguished om chronic portal systemic encephalopathy by the ecessive inheritance the age-incidence the absence of luctuation in the signs the Kayser Fleischer rings the mino-aciduria and the abnormal copper metabolism low serum-copper and high urinary copper values) A pecific defect of cæruloplasmin allowed unstable copper o be deposited in the tissues and this produced the clinical features of the disease Copper could not be excluded from the diet but potassium sulphide diminished absorption The best treatment was dimercaprol potassium sulphide and a high protein diet and this might prevent deterioration in asymptomatic cases.

Summing up Professor McMichael said he was always interested in those points which failed to conform to an accepted theory for he felt that they often held vital clues The conference had been a success and he referred particularly to the considerable contributions by Dr Sherlock

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Public Health

MALIGNANT DISEASE OF THE RESPIRATORY SYSTEM

A STATISTICAL SURVEY

F L BRADSHAW

F.I.A

THIS survey was prompted by Dr Evarts Graham's recent lecture[1] on the Ætiology of Bronchogenic Carcinoma. He based his observations largely on statistical material obtained in the United States and it seemed likely that a similar study of statistics for England and Wales might give rather different results since the average age of our population is appreciably greater

All the figures are taken from part I of the Registrar General's annual statistical reviews Descriptions of cancer—i.e., malignant neoplasms—and the six broad classifications of its sites are those given in the review for 1952 The survey covers the twenty year period 1932–1952 using figures for selected years only Population statistics between 1940 and 1948 were disturbed by the war and accordingly it seemed better to use figures for three of the early years of the period and those for the last five years These, together with figures for two years in the middle of the period provide a reasonably accurate picture of the general trend between 1932 and 1952

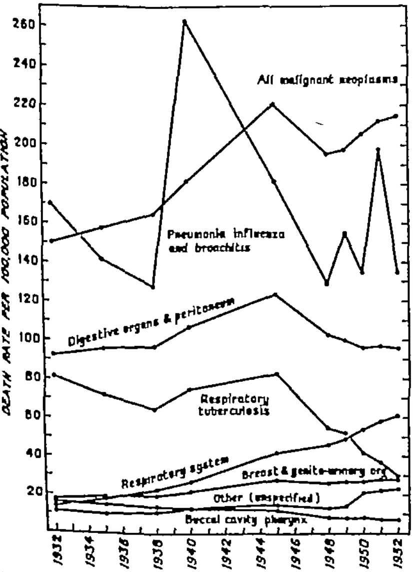

Fig 1—Deaths per 100 000 population in England and Wales from malignant neoplasms and diseases of the respiratory system from 1932 to 1952.

COMPARISON WITH OTHER DISEASES

Fig 1 shows the number of deaths per 100 000 of the male population of England and Wales from cancer and certain diseases of the respiratory system. The latter are shown so as to bring the graph broadly into line with that in Dr Graham's fig 1 The different age distribution in this country explains why our death rates are very much higher than those of the United States The fall in the death rate for respiratory tuberculosis from over 80 to 30 roughly corresponds to that in the United States The curve relating to pneumonia influenza and bronchitis is difficult to interpret owing to its violent fluctuations yet here too there has undoubtedly been a fall though a very much smaller one than in the United States

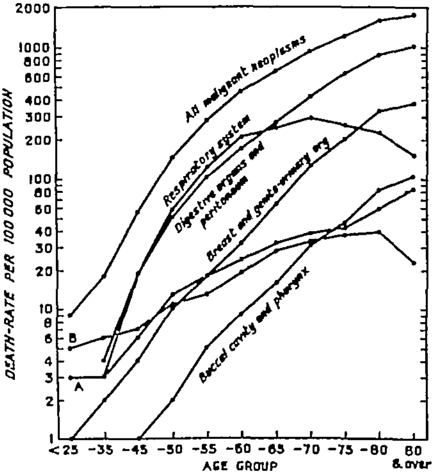

Fig 2—Deaths per 100,000 population in England and Wales from malignant neoplasms in 1952 (by age-groups) (A—other unspecified sites ; B—lymphatic and hæmatopoietic tissues.)

The curves for malignant neoplasms show that the steepest rise in death rates has been in cancer of the respiratory system Cancer of the digestive organs is however still the greatest destroyer of life Cancer of the breast and of the genito-urinary organs shows a steady increase and cancer of other and unspecified organs shows a rapid increase in the last five years Cancer of the buccal cavity and pharynx alone shows a decline

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[1] Graham, E. A *Lancet* 1954 i, 1305

Fig 2 is constructed to show the *malignancy*, as distinct from the destructiveness, of the various cancer groups Assuming that senility is a considerable factor in all deaths after the age of 70, the malignancy of a disease may be assessed by its destruction of life before that age On this basis, cancer of the respiratory system is the most malignant of all the cancer groups, though followed closely by cancer of the digestive organs

The peculiar bend in the curve for cancer of the respiratory system, which results in it crossing the curve for cancer of the digestive organs after age 60, explains the lower over all death rate from respiratory cancer The two curves plotting cancer of other and unspecified sites, and cancer of the breast and genito urinary organs, exhibit similar features the former shows greater malignancy and the latter a higher over all death rate Cancer of the buccal cavity and pharynx (which has the lowest death rate of any of the groups) is lowest also in malignancy

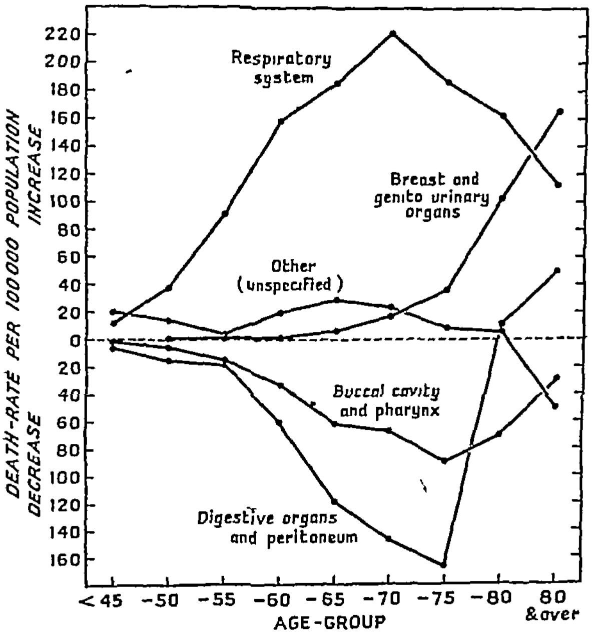

Fig 3—Changes in age-group death rates per 100 000 from various malignant neoplasms between 1932 and 1952.

Fig 2 shows the relative malignancies of the cancer groups in 1952 In 1932 these relative malignancies were very different, and fig 3 has been constructed to show broadly the changes which have taken place It shows for each of the groups the increase or decrease in the death rate during the twenty year period for all ages up to 45, and thereafter in the quinquennial age groups used in fig 2

Defining malignancy, as before, as the number of deaths caused before the age of 70, cancer of the respiratory system shows by far the largest increase in malignancy, whereas cancer of the digestive system—its present runner up in this respect—shows by far the biggest decrease Cancer of other and unspecified sites shows an appreciable increase in malignancy For cancer of the breast and genito urinary organs the increase is practically negligible Cancer of the buccal cavity shows a decrease throughout the whole of life

Our experience of cancer of the respiratory system follows very closely that of the male population of the United States, as revealed in Dr Graham's fig 1 During the period under review there was a very serious increase in the malignancy of cancer of this site On r hand, our experience of cancer of all the other

TABLE I—DEATHS PER 100,000 FROM CANCER AND RESPIRA DISEASES, 1952 COMPARISON BY SEX

Age and sex	Malignant neoplasms								Respiratory system
	All sites	Buccal cavity	Digestive organs	Respiratory system	Breast and genitalia	Urinary organs	Other and unspecified sites	Lymphatic and hæmatopoietic tissue	Tuberculosis
All ages									
Men	215	7	96	61	16	12	12	11	31
Women	185	3	81	11	67	5	10	8	13
Under 70									
Men	141	4	54	51	6	7	9	10	13
Women	117	2	40	8	50	3	7	7	12

sites is not unsatisfactory, because though the death-ra per 100,000 of our male population has increased quantitatively from 136 to 154, the malignancy has been reduced, and the corresponding death rate for ages under 70 has fallen from 92 to 90—a small reduction, but one of considerable economic, and no doubt medical significance

SEX DIFFERENCE

Another fact mentioned by Dr Graham is that bronchogenic carcinoma is about 6 times commoner *in men than in women This parallels our experience*: over-all and under-70 death rates for men in England and Wales are respectively $5^1/_2$ times and $6^1/_2$ times those for women Nor is the higher frequency of cancer in men confined to this one site it extends to all sites excepting only the breast and genital organs Moreover the over all death-rate from all diseases of the respiratory system (including tuberculosis but excluding cancer) was in 1952, about $1^3/_4$ times greater in men than in women and the death-rate for men under 70 was more than double that of women These figures, with those relating to cancer, are given in detail in table I

EFFECT OF VULNERABILITY

For some reason, men are more vulnerable to cancer on the one hand and to diseases of the respiratory system on the other, and these two facts may partly explain the high lung cancer death rate in men Moreover, the statistics show that during the period under review there has been a substantial reduction in both the destructiveness and malignancy amongst men

TABLE II—DEATHS DUE TO MALIGNANT NEOPLASMS IN MALE 1948–53

Causes of death	1948	1949	1950	1951	1952
All malignant neoplasms					
Total deaths	40,026	40 772	43 570	44,632	45 429
Death rate per 100 000	190	198	206	212	215
,, below 70	128	128	136	138	141
,, at 70 and over	1326	1354	1404	1441	1443
Malignant neoplasms of digestive organs					
Total deaths in year	20,970	20,629	20,420	20,405	20,175
Death rate per 100 000	103	100	96	97	96
,, ,, below 70	61	59	55	55	54
,, at 70 and over	796	782	782	790	761
Malignant neoplasms of respiratory system					
Total deaths in year	9,465	10,163	11,340	12 237	12,971
Death rate per 100 000	46	49	54	58	61
,, below 70	40	42	45	49	51
,, at 70 and over	146	168	194	215	227
Percentage of deaths below 70	82	$80^1/_2$	$79^1/_2$	79	79
Percentage of deaths at 70 and over	18	$19^1/_2$	$20^1/_2$	21	21

ll diseases of the respiratory system except cancer , so he considerable increase in lung cancer may be the esult of better treatment of other lung diseases The tatistics show that the reduction in the over all death ate for men from all diseases of the respiratory system, other than cancer, is 53 per 100 000 and in the death ate for ages under 70 is 99 per 100,000 Corresponding ncreases in the death rates from cancer of the respiratory ystem are 47 and 39 respectively

How far the present high death rate of men from cancer of the respiratory system is attributable, on the one hand, to the tobacco habit and, on the other hand to their general *vulnerability to cancer only future* research will decide What this survey does indicate is that either of these factors could explain the increased incidence of respiratory cancer since 1932

THE 1953 FIGURES

Since I *prepared these figures, statistics for 1953* have been published Table II covers the main features of the survey of the statistics for males during the six years ending with 1953 The trends already observed are continuing but there are certain aspects of the 1953 figures which give cause for satisfaction

(1) The over all death rate from cancer of all sites has fallen from 215 to 214 per 100 000 male population. The amount of the decrease is insignificant yet it is the first time a fall has been recorded Also the malignancy—i e , the death rate below age 70—shows definite signs of slowing up it has increased by only 1 per 100 000 whereas the average yearly increase in the previous period was nearer 5 per 100 000

(2) For cancer of the digestive organs, the fall in all death rates has continued Cancer of this site is still the greatest destroyer of life though in its malignancy it is surpassed for the first time in 1953 by cancer of the respiratory system

(3) It is difficult to find any satisfactory feature in the figures for cancer of the respiratory system yet here too there is a slowing up *in* the malignant death rate This is not apparent from the death rates themselves, but can be seen from the last two lines of table II which give the percen age of deaths below and above age 70 Over the six years he proportion below age 70 has steadily declined

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LONDON'S WATER-SUPPLY

THE 35th report of the director of water examination Metropolitan Water Board, covers the six years 1947–52 and the water-supply to a sixth of the population of this country This is Colonel E F W Mackenzie s last report as director, and it bears throughout the marks of his wisdom experience and guidance through all the vicissitudes of war and of post-war reconstruction His earlier report, the 34th covered the eight years 1939–46 so that the second volume completes the account of his distinguished service with the board It is full of material of unique value to science far beyond the narrower interests of public health or water engineering

BIOLOGICAL DIFFICULTIES

The biological section deals with some of the broader conceptions of exploiting the natural water sources in the London basin Many of the reservoirs have accumulated sediment for over fifty years with some incidental small loss of storage capacity and retention time but the deposits have affected the algal fertility particularly during the summer when the reducing substances on the bottom tend to deoxygenate the lower layers of the water and impose chemical stratification to complicate the natural thermal stratification The seasonal overturns and the disturbance of stratification by rough weather are liable to embarrass the filters with algal scum and impart to the drinking-water unpleasant tastes which occasionally defy all treatment Constant assessment of the algal state and a certain amount of ingenious juggling with variable level draw-offs, kept these inconveniences to a minimum, but at other times it was necessary to resort to the more expensive application of copper-sulphate algicides. Colonel Mackenzie wonders whether a more biological outlook on the operation of reservoirs might have an important influence in reducing the financial loss and the nuisances resulting from excessive growths He seems to have been spared the problems of toxic pesticides and agricultural weed killers which are beginning to worry some users of overground water-supplies. The control of midges around the reservoirs has been much less effective; luckily they are non biting chironomidæ, and the local population are advised to live in philosophical symbiosis with the invaders

BACTERIAL CONTAMINATION

Medical interest flows naturally from the wider aspects of biology into the bacteriological section of the report. Some 45,000 samples have been examined each year and the chief interest centres upon the traditional indicator organism *Escherichia coli* Two of the many practical observations were that 99 2% of all the *E coli* specimens received were obtained in the first eighteen hours incubation, and that most of the false presumptives were due to *Clostridium welchii*, particularly in chlorinated waters Laboratory techniques for the rapid identification of *E coli* are discussed in detail before the report passes on to more considerations of public health. It is startling to realise that the 1931 milk borne epidemic of paratyphoid B in Epping is still reflected in the sewage effluent The readiness with which the organism can be recovered indicates the local persistence of a high symptomless carrier rate Such findings illustrate the importance of routine medical examination of all waterworks employees who might contaminate public water supplies and of *re-examination* after any suspicious illness The preliminary sorting was done with Vi agglutination tests. 2502 employees were examined and 7 3% showed Vi agglutination. All the positive reactors had at least three stool and urine examinations, and 3 men even endured duodenal intubation for examination of their juices. No enteric organisms were recovered The re-examination of 1817 employees after suspicious illnesses revealed 28 cases carrying pathogens, mostly *Shigella sonnei* and *Salmonella typhimurium* Such routine precautions are a counsel of perfection, but they are difficult to apply in smaller undertakings and with outside contractors labour

CHEMICAL CONTENT

The chemical section of the report deals in detail with the changing methods for estimating the hardness and other inorganic constituents of the waters, and goes on to describe an interesting little piece of detective work on the River Lea to incriminate the springs in the bed as the cause of wide variation in hardness in different reaches of the river Investigation of the average natural fluorine content in 50 sources of London s water-supply in 1949 showed that the northern wells contained much more fluorine than the southern group Those in direct supply included East Ham with 1 08 parts per million (p p m) Hadley Road with 1 11 p p m and Ferry Lane with 0·91 p p.m., whereas most of the Kent wells contained less than 0 05 p p m The differences may be of some significance to the current investigations *into fluoridation of public water-supplies. This* section of the report ends with a description of the use of disodium hydrogen phosphate ($Na_2 HPO_4, 12H_2O$) as a tracer for detecting the flow of underground waters, particularly where pollution is suspected The method was found to have many advantages over the use of colouring materials, common salt or lithium chloride provided that laboratory facilities are readily available

CLARIFICATION

Research into the clarification of river derived supplies was continued in the full-scale experimental plant at Kempton Park The problem was not so much concerned with inert matter which settled to the reservoir floor but with the removal of suspended algæ. The experiment proceeded in three stages using respectively al sulphate, iron coagulants, and aluminium sulphate assisted by activated silica The relative advantages between slow sand filtration and coagulation processes remain to be assessed after extended trials Investigation was also carried out in the use of aluminium pipes and domestic utensils. Such pipes are discouraged, but aluminium utensils are reasonably satisfactory provided that they are first well washed out and then allowed to develop their own protective coating

CHLORINATION

The post-war years have seen radical changes in the technique of chlorination The longstanding practice of chloramine treatment has given place to superchlorination, of a degree where the dose is more than sufficient to disinfect the water without however satisfying the full chlorine demand The element of dechlorination can therefore be said to be self-induced, and in recent years there has been virtually no chlorine in the water supplied to London A dose of 1 p p m to the filtered water yields a residual of 0 3 to 0 4 p p m within a few minutes, and disappears during an hour's contact The necessity for prechlorination is obviated, and the bacteriological and physical quality of the water passed to supply is better than ever before, besides saving over £12,000 a year in chemicals A progressive policy has been carried out at all the wells for installing contact tanks, which incidentally serve as balancing tanks, to the combined joy of both the medical and the engineering interests

EMERGENCIES

The importance of these safeguards is emphasised by accounts of the accidents which have happened during the period covered by the report The flooding of the Lea Bridge works in 1947 temporarily deprived a large area of east London of its water-supply and presented many difficulties in restoring a safe supply The leakage of the public sewer into the Crayford well in 1950 was an event which would have had very serious consequences had the control measures not been so efficient But in spite of all the care exercised at the waterworks, the human element in the distribution can defeat the defences by unauthorised cross-connections Instances are described of steam, and even paraffin oil, coming out of consumers' cold-water taps, as well as of cross connections with impure supplies Constant inspection is the only answer to these risks, which are fortunately rare

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Population Changes

The United Nations Statistical Office has just published its *Demographic Yearbook* for 1954,[1] which gives the latest news of the world's population trends The tremendous task of gathering, analysing, and arranging details from all over the world has been accomplished with striking speed and many 1953 figures are included Moreover, the statisticians have added an assessment of the limitations of each set of data, taking into account, for example, comparability and differences introduced by variations in the statistical habits of the countries concerned

The section on births includes tables setting out the number and rate of births classified according to the age of the mother The birth-rate per 1000 population is lowest in Western Europe (from 15 to 20), and one of the highest 1953 rates was in Burma (49 2) The 1953 birth-rate in the United States was 24 7, almost identical with the provisional rate for India in 1952 (24 8) and rather more than the 1953 rate for Japan (21 5) The tables in the yearbook illustrate how in the past thirty years birth-rates in Western Europe have fallen greatly, the lowest points being reached just before and during the late war

For this country the tables dealing with the age of mothers show that younger women are nowadays producing more children than they did before the war one of the chief reasons is that more women are having children in the first few years after marriage than was the case before the war

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[1] Demographic Yearbook 1954 United Nations, New York Pp 729 45s Obtainable from H.M Stationery Office P O Box 569 London S E 1

In England Now

A Running Commentary by Peripatetic Correspon

OUR medical painters are gaining in competence have they lost in the process some of the careless which made their earlier shows so lively ? The exhibition of the Medical Art Society, in progress Walker's Galleries[1] until April 30, is relatively sedate A B Hewlett's brilliant greens and meticulous beckon in the first room and this time he has achieved in *The Station Approach*, a really fascinating pattern—of garden, roadway, bold pink signal-box, and rolling hills into which a neat cow and a neater railway train are nosing their way, while a man in the foreground has leisure to drink beer He has certainly earned a drink, for every plant in his garden (possibly Eden) is flourishing in exact pace with its neighbours, and there is not a weed to be seen I was disconcerted, however, to find that I could not, for once, identify the flowers in the border chrysanthemums perhaps ? We must hope that Hewlett is not losing his usually (and unusually) firm grip of his subject Very different in technique is F Forty's *Forteleza da Sao Joao de Estoril*, where the pale yellow building, in its circle of bluish yaccas, seems to have floated down from the heat-shaken blue of the sky, In G Crosby's *Provençal Vegetable Stall*, yellow heat streaming beyond a dark archway tells of another hot day , but R A Beaver's *Playground, Cumberland Market* is very cold indeed The little black figures against the pale colours of this amusing painting seem to be crying out for pen-and-wash, however, rather than oils, T Holmes Sellors has noticed some pleasing reflections in his window, in *Interior at Night*, and Isabel Wilson has done a useful best to find colour in the interminable fastnesses of *Colcherne Road* H Elliott Blake has abundant colour to hand in *La Petite Auberge*, and has used it with discrimination and skill A J Edelsten's *East Lyn Valley*, with its warm-coloured earth and pale grass, and B N Brooke's dark old lock-gates in the shadowy dun countryside of *Lapworth* both gave me pleasure , and so did the small bright *Storm over Meil* and *Officer's Mess, Maynamati* of J F Stokes In *Still Life*, N Ashton has got a raw cabbage and an onion to the life, rather consciously grouped with half a glass of white wine and some other vegetables

Portraits make a good showing this year , and the palm, as far as I am concerned, goes to E W Peet for his painting of *Dr E W Ainley Walker* Sir Philip Manson-Bahr, president of the society, has been splendidly drawn by René Michelmore, who is also responsible for two other good portraits—*Lisa* and *Head of a Negro* The catalogue suggests that Josephine Roth's drawings of *J D Allan Gray, Esq , T.D , F R C P E , D P H* , and of *Horace Joules, Esq , M D , F R C P* , depend for interest on a plethora of diplomas, but they are, in fact, very good crayon portraits , and R O'Meara's yellow-lighted side view of *Dr R N McKinstry* is another clever and agreeable little likeness There was not much abstract art about I suppose our profession is not much given to abstractions N Newman in *Reverie* has attempted, it seems, a rapid review of Greek art and the art of Henry Moore and Salvador Dali It is perhaps not surprising that the partners in this ambitious programme had failed to compose themselves comfortably in the space available Among the few three dimensional exhibits there is a pleasing *Bitch and Pups* in glazed pottery by A. C Dalzell and a chunky little *Morris Dancer* on a hobby horse, carved in wood by G Sparrow Sparrow, it may be remembered, is the unique humorist who likes drawing his own hunting prints He has two splendid ones in this time—*Meet of Royal Buckhounds, 1810*, and *Tommy's Stables* Both are nicely mounted in old maple frames, and would make a handsome addition to any lady or gentleman's parlour

* * *

The Salk poliomyelitis vaccine has arrived Even before details of the elaborate and, I believe, careful experimental work have been presented to any competent scientific society, television, radio, banner press headlines, and 4 complete pages of the *New York Times* have informed the public of its wonders The names of Salk and Jenner are on the lips of countless citizens. Already anxious parents are demanding the vaccine for their children and worried administrators are requesting Presidential action to ensure its fair distribution It is difficult for laymen here to see the risks of poliomyelitis in their correct perspective There are 16,000 cases a year; a quarter of the cases have paralytic symptoms and of these only a further quarter have permanent paralytic sequelæ The risk of a child being killed or maimed by car accidents is incomparably greater

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[1] 118 New Bond Street, London, W 1

When I arrived in New York I saw everywhere huge posters which told me ' Save your child from Leukæmia—give to the American Cancer Society It was fairly easy for me to see this appeal in perspective but a great deal less easy for the average parent The research foundations of America support an enormous amount of valuable and useful research, and in turn they are most generously supported by the public Unfortunately the public is more generous when its emotions have been stirred; and I don't myself believe that support for research should be obtained at the cost of arousing unnecessary fear

* * *

The peripatetic correspondent[1] who confessed to his ignorance of the Heat Barrier made the usual mistake of failing to consult the literature This obviously is the flame belt that divides the two hemispheres of Venus and allowed the simultaneous development of Theron and Treen civilisations. It was first fully described by Dare et al[2] and subsequent references in the literature are too numerous to quote Should the peripatetic correspondent have difficulty in obtaining the original paper an arrangement might be reached with the progeny of the present writer for the loan or exchange (with similar scientific material) of a genuine first edition

* * *

Our ward telephone rang the other day—it was a lady asking how Mrs Colby Brown was getting on after her appendicectomy Sister replied that the patient was doing famously and would shortly be sent home. Asked for her name, the lady replied Well Sister, this is Mrs. Colby Brown You're all so busy I just don't like to bother you on the ward rounds.

* * *

Last week I bought a book on motoring The chapter on Motor-cars and Health is by Sir Henry Thompson, F.R.C.S In it he writes:

> "The easy jolting which occurs when a motor-car is driven at a fair speed over the highway conduces to a healthy agitation; it acts on the liver to use a popular phrase which means only that it aids the peristaltic movements of the bowels and promotes the performance of their functions; thus accomplishing the good in this respect which arises from riding on horseback.

The date of publication is 1902

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SIR JOHN BLAND SUTTON

Born April 21 1855

Rebellious spirit thou didst fight
Thy way from humbleness to might
And wealth and fame Boldly thy knife
To ailing women gave new life
With lion's heart challenging fate
The pelvic surgeon didst create

Dry teaching didst enliven and beguile
With Ligaments and Tumours, and the while
Thy wit did echo and thy cockney quips
Delightedly from students' lips

Wand'ring Elysian fields tonight
With Jockie Hunter kindred spright
And purring Tim with beady eyes,
Affection blended with surprise

The man we loved—remote and rare
A London sparrow in the air

W. R. BETT

Letters to the Editor

DEALING WITH DISASTER

SIR,—You do a much required service in drawing attention to the need for adequate arrangements for dealing with disasters[1] But surely you are wrong in stating that there are few areas in the United Kingdom not within easy reach of big hospitals? Reference to any railway map and to reports of aircraft accidents will show how wrong you are

In spite of the last sentence in your article of Feb 5, your antagonistic attitude to resuscitation on the spot has two serious dangers. First, you may prejudice inexperienced practitioners against resuscitation before evacuation Second, you may well be quoted (or misquoted) by lay administrators and committee members as an authority against making adequate provision for resuscitation at the scene of disasters

The indications for transfusion &c, before evacuation can only be judged by the medical man treating the patient, with due regard to the patient's injuries and condition and to the time and methods involved in evacuation Rather than your lukewarm final sentence you should write 'Arrangements for immediate transfusion *must* be included in the plan they may not be needed but when they are they will then save life '

R.A.F. Hospital
Changi Singapore

J B ROSS

MENTAL NURSING ANALYSED

SIR,—In your leading article of April 9 you discuss the study of the function and training of mental nurses carried out at the Bethlem Royal and Maudsley Hospitals in 1951–52

Among other points you draw attention to the discrepancy between theory taught and practical work done by student nurses in mental hospitals, particularly in their first year

This is an old problem which has been relieved a little by a new syllabus which contains the importance of mental and physical health to the individual the family and the community under the broad heading personal and communal health The preliminary syllabus however is still concerned mainly with the care of physical conditions and is therefore inappropriate for mental nurses. This is because it is assumed that the care of the sick in body is basic nursing while the care of the sick in mind is not and that basic nursing should be learned before something which is thought of as specialised Another reason is that the practice of teaching the preliminary syllabus in the first year (to allow students to take the examination as soon as possible) has hardened into tradition Most mental nurses and their tutors do not agree either with the assumptions or the practice but they accept the tradition bad as it is because the preliminary training school does allow an uninterrupted period in which to teach the preliminary subjects—an opportunity which for most tutors does not recur

There is a simple way out—namely a change in the order in which the syllabus is taken The purpose of the preliminary training school is to prepare a nurse for her work in the wards. The minimum period required is 8 weeks, some part of each day being spent in the wards These weeks should be spent in teaching mental nursing understanding and managing patients, and ward routines and practices. During the following 9 to 12 months psychiatry and mental nursing should be taught The subjects in the preliminary syllabus with their bias towards physical nursing could be taught in the second year together with the medical and surgical nursing usually taught at this time The preliminary examination could be taken at the end of the *second year* when the students would have the knowledge and practice and therefore the confidence to pass The only stipulation the General Nursing Council makes is that the preliminary examination shall be taken before the final. The third year should be occupied by advanced psychiatric nursing and before taking the final examination a short revision of the nursing of physically ill patients

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[1] *Lancet* April 9, 1955, p 760
[2] Dare D., Hank, et Pierre *Eagle* July 1950

[1] *Lancet* 1954 i 1003; *Ibid* Feb 5 1955 p 205

The conflict between the needs of the hospital for service and of the student for education is another old problem, one solution to which is suggested by reading the Bethlem and Maudsley study

This compares two ways of arranging nurses' hours in mental hospitals—the so called long day and the shift system The long day is said to need fewer staff but it is very tiring for the nurses The shift system may need more staff but it can be arranged with overlapping time which could be used by students for lectures and private study It would be possible to have the best of both systems by letting the trained, auxiliary, and part time staff work the long day (or night), and the students work overlapping shifts This would allow the wards to be staffed by those not in training at the times when the students' shifts overlapped, and it would allow the students to have some part of every day for study

These simple changes could remove two of the greatest difficulties in the training of mental nurses and help to smooth the furrows from the tutors' brows

R M N

PHARMACOLOGY OF RESERPINE

SIR,—Oversimplification of complex problems by postulation is an old philosophical method which despite its age is unacceptable in science Your leading article of March 12 contained a striking example You postulated that reserpine was "the active alkaloid" of *Rauwolfia serpentina*, and then felt free to treat all data accumulated on any rauwolfia medication as if they had been obtained by using reserpine

1 Actually there are at least five generically different preparations of rauwolfia

(*a*) Ground rauwolfia root containing reserpine like (brady cardia, hypotension, sedation producing), yohimbine like, and numerous other alkaloids possibly potent in as yet unassessed desirable or undesirable ways The fact that ground crude root preparations can be made from any of more than one hundred varieties of rauwolfia from all over the world (varieties which have manifestly different constituents), and the fact that even within the most desired species (*Rauwolfia serpentina*) there exist differences between roots from Siam, Burma, Thailand, and India, make lumping of data hazardous There are rauwolfias which apparently contain no reserpine (*Rauwolfia paraensis*, *Rauwolfia cambodiana*, and *Rauwolfia caffra*)

(*b*) The alseroxylon fraction, 'Rauwiloid,' an alkaloidal extract known to be free of yohimbine like alkaloids, known to contain reserpine, rescinnamine, and other potent reserpine-like materials, guaranteed by its manufacturer to be made only from *Rauwolfia serpentina* of Indian origin

(*c*) Reserpine, a single alkaloid, difficult to purify, extracted from any of *Rauwolfia heterophylla* (South American), *Rauwolfia hirsuta* (South American), *Rauwolfia vomitoria* (West Africa), *Rauwolfia canescens* (India), *Rauwolfia serpentina* (India) The contaminant alkaloids vary with the root of origin, and the difficulty of being sure that the sample is over 80% reserpine varies also This alkaloid does not produce adrenergic blockade at any dose It is the tri methoxy benzoic ester of methyl reserpate

(*d*) Rescinnamine, a single alkaloid whose structure is thought to be the tri methoxy cinnamic ester of methyl reserpate, found to date only in *Rauwolfia serpentina* While rescinnamine is not presently available for purchase, a considerable clinical usage has revealed that it is distinctly less sedative than reserpine, though pharmacologically both quantitatively and by its general potency, it is reserpine like

(*e*) Canescine, isolated from *Rauwolfia canescens*, is probably 11 desmethoxy reserpine Animal work has established that canescine is a member of the reserpine group, but clinical experience is not wide enough as yet to permit any guess as to its properties as applied to human disease

2 Present clinical indications suggest that the mixed alkaloids without the yohimbine component (*b* above) present a better balanced action less critical in dosage and somewhat less threatened with side actions Only further clinical work will establish this and elucidate reasons for it

Examination of the references cited in your lea article will show that numbers 1, 2, 4, 5, 6, 25, and were concerned with preparation (*a*), 6, 8, 10, 21, and were concerned with preparation (*b*), and the rest with preparation (*c*) Few papers exist on (*d*) and (*e*)[35-41]

Meanwhile, oversimplification of the situation by postulating that reserpine is clinically and pharmacologically typical of all rauwolfia preparations can only interfere with proper stimulation of investigators to clarify further the enigmas involved

References 1–34 are contained in the leading article (March 12, 1955, p 548)

Los Angeles, California, U S A GEORGE L MAISON

⁂ Dr Maison earns our thanks for his valuable survey of rauwolfia preparations In our leading article we tried to resolve confusion caused by the introduction of different rauwolfia preparations, and in referring briefly t the clinical use of rauwolfia we did not distinguish between experience with different preparations, but, in fact, all but three of the papers cited on the experimental pharmacology of reserpine, with which we were principally concerned, dealt with pure preparations of the alkaloid —ED L

GENETIC EFFECTS OF THERMONUCLEAR EXPLOSIONS

SIR,—Biologists tell us that mutations followed by selection have been the chief factors in improving living species Yet in current discussion of the genetic effects of radiation, it is widely assumed that any increase in the human mutation rate must be harmful to the species Are we to infer that for mankind alone selection is impossible? Or is the human race already so perfect that further improvement is inconceivable?

The public have had ample warning of harmful mutants Should not equal stress be laid on the relatively rare favourable mutations which could be of great benefit to the race?

Wendover R B BOURDILLON

REGISTRARS AND REGISTRARS

SIR,—At present some medical registrars are quite obviously to be considered solely as trainees There is, for example, the professorial unit type, who assists in the investigations and treatment of a handful of patients with obscure maladies, aided by six or so colleagues of similar status, and adequately supervised by his eminent chiefs He will have much spare time in which to browse in the university library or spend in learned discussion From time to time he may take part in the preparation of articles of high academic merit for learned journals

Other registrars find themselves so busy with the day chores that academic achievement is out of the question Consider, for instance, the lot of the average registrar at a provincial chest clinic, who shares clinic sessions and domiciliary visits equally with his consultant chest physician and the S H M O, and who deputises for the radiographer, clerk, or health visitor as occasion requires Indeed, what is meant to be the proper function of the grade has been the subject of much recent controversy

Clearly the current title of registrar covers no more a homogeneous group of appointments than does, say, the military rank of staff captain It is worth noting however that the latter designation is rarely used by itself—a letter is usually suffixed in parenthesis to show more exactly the duties of the gentleman in question

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35 Cronheim G, et al *Proc Soc exp Biol N Y* 1954, 86 1
36 Cronheim G, Toekes, I M *J Pharmacol* 1955 113 13
37 Klohs, M W et al *J Amer chem Soc* 1954 76 2843
38 Hershberger R., Hughes, W, Dennis, E *Proc Amer Fed clin Res* 1955 3, 71
39 Klohs M W, et al *J Amer chem Soc* (in the press).
40 Stoll A, Hofman A *Ibid* 1955 77 820
41 Cronheim, G, Orcutt, J, Toekes, I M Unpublished

Thus an officer in the intelligence branch would be labelled staff-captain (I) and the corresponding one in the medical department staff-captain (M)

It is suggested to the Strachan Committee that they now recommend two subgrades of registrar those who work strenuously at peripheral hospitals to be known as working registrars or registrars (W), and those who train leisurely at the teaching hospitals to be labelled registrars (T)

REGISTRAR (W PLUS)

CLONAL AGEING AND CANCER

SIR,—Your leader of March 26 which I found most interesting suggested to me a possible explanation for something which has always puzzled me—namely how it is that carcinogenic agents such as cigarette smoke need to act for many years before their effects appear

If the carcinogen acted directly upon the cell nucleus or cell protein it should like other poisons act at once If, on the other hand its action depended (like radiation) upon some statistical chance of reaching the cell nucleus, then some persons would be affected early and others late in a continuous series

But if the carcinogen simply acts by causing cells to proliferate so that instead of dividing by mitosis x times in 20 years, they have been stimulated to divide $x \times y$ times ($y > 1$) and if, as Sonneborn seems to have shown in paramecium, the chromosomal substance duplicates more and more inaccurately as the number of divisions is increased and if this kind of nuclear aberration could cause a malignant change in the cell the reason for the latent period would be explained.

I write in complete ignorance as to whether there could be anything in this theory in the hope that some more knowledgeable reader will enlighten me Perhaps the effect of carcinogens on cell multiplication is already well known but when I recently asked a well known expert in cancer research the cause of the latent period in the action of carcinogens he was unable to give me an explanation

Manchester ROBERT PLATT

ENURESIS

SIR—In your leading article of Feb 19 you emphasise again the importance of considering all factors bearing on this elusive but widespread syndrome There can be few who would not agree that each case must be studied as an individual problem or that in most cases there would seem on investigation to be multiple ætiological factors I would however draw attention to one or two observations made elsewhere

In considering the establishment of a simple conditioned reflex Crosby[1] describes a method which aims at extinguishing any conditioned responses which facilitate micturition and at reinforcing the natural method of building up inhibitory tone

Discussing the use of the amphetamine drugs you mention the lightening of sleep but do not discuss the possibility that the action may involve 'alerting' of the cerebral cortex via the reticular diffusion system[2] and that such action need not proceed to arousal but can yet activate cortical reception and the intensity of the subsequent inhibition impulse[3]

In considering the phenomenon of nocturnal enuresis the concept of delayed or inept cerebral adaptation[4,5] should perhaps be borne in mind.

Taunton R SESSIONS HODGE.

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[1] Crosby N D *Med J Aust* 1950 ii 533
[2] Bradley I B Ph D thesis Birmingham University 1952
[3] Higgins, T T., Williams D I., Nash D F E. *Urology of Childhood* London 1951
[4] Sessions Hodge R, Hutchings H M *Arch. Dis Childh.* 1952 27 498
[5] Bett W R., Howells, L H Macdonald A D *Amphetamine in Clinical Medicine* Edinburgh, 1955

RADIOLOGY IN THE MANAGEMENT OF ANTERIOR PLACENTA PRÆVIA

SIR,—Mr Russell and Dr Warrick in their commendable article last week do well to emphasise the potential dangers to the fœtus from cæsarean section in the anterior type of placenta prævia and in pointing out how the extra information gained from soft tissue placentography may be used in making the operation safer for the fœtus

I am sure however, that they can make the operation safer still for both fœtus and mother by avoiding examination under anæsthesia altogether when there is such good evidence (both radiological and clinical) of major placenta prævia, and proceeding to cæsarean section without it In this way the patient will not be made to run the extra risk of serious bleeding caused by percervical examination; the fœtus too, will not be subjected to anæsthesia for longer than is necessary

When precise soft-tissue placentography and the clinical findings both point to a major degree of placenta prævia, not only is there no need to use the hazardous digital examination of the lower segment but there is every reason for avoiding it This is only one of the important contributions that soft-tissue placentography has made to the management of placenta prævia

The London Hospital E 1 ROBERT PERCIVAL.

COWPOX IN MAN

SIR,—The paper by Dr Bernard Laurance (April 9) provides a timely reminder about the wealth of material still awaiting investigation in the sphere of comparative medicine—the comparative medicine near at hand in everyday life In the outbreak he describes there are implications involving medicine surgery pathology, and epidemiology, any one of which subjects could well provide a matter for separate study, while such outbreaks seem to present special opportunities for further studies on viruses

I suppose there are so few references in the literature

RUPTURE OF THE DUODENAL STUMP AFTER GASTRECTOMY

SIR,—I would like to give strong support to the contention by Mr Henson in his article of March 19 In my experience this complication has twice followed obstruction to the afferent loop and there is little doubt in my mind that, except in the cases where closure is frankly inadequate, this is the usual sequence of events That the complication may occur is, among other reasons, a good one for avoiding the Polya operation in gastric ulcer wherever possible

In duodenal ulcer, where the operation has its main use, the technique which avoids the use of occluding clamps of the Lane type is the surest and safest way of making an anastomosis unlikely to produce obstruction A full-width anastomosis can be used with little risk of contamination or bleeding if the stomach is divided with high frequency diathermy, provided preparation has been good beforehand

There is little risk of contaminating the peritoneal cavity if the Finsterer type of operation is preferred, The lesser curve part of the stomach can easily be closed using the Maingot clamp, and an anastomosis carried out without the use of any further clamps

In my experience any contamination that may result is negligible and it is possible for the less experienced surgeon to ensure a safe stoma and hence a safe duodenal stump

Kimberley, British Columbia C R NEVE

CONTINUOUS INTRAMUSCULAR OXYTOCIN

SIR,—Continuous intravenous oxytocin has been shown to be a powerful therapeutic weapon in many obstetric problems demanding stimulation of the uterus By carefully regulating the rate of administration, an optimal uterine response can be obtained and normal progressive labour effected [1]

The presence of an intravenous needle, however, is not without its disadvantages Variations in the position of the needle relative to the heart will influence the rate of flow, movement of the arm may compress the vein or occlude the end of the needle and this can only be overcome by splinting, trauma to the vein wall and the prolonged administration of isotonic solutions, especially glucose, often result in local thrombosis, and, because the patient is immobilised and her arm is splinted, her morale falls should it be necessary to continue the intravenous drip for more than nine hours To avoid these disadvantages oxytocin given by continuous intramuscular drip was tried and has been found to be highly satisfactory

10–15 units of oxytocin is added to 1 pint of normal saline solution The needle of a standard intravenous giving set is replaced by a no 12 intramuscular needle, which is then inserted under strict aseptic precautions deep to the ilio tibial tract into the vastus lateralis muscle in the middle third of the thigh 1000 Benger units (450 turbidity reducing units) of hyaluronidase dissolved in 1 ml of normal saline solution is injected into the rubber tubing near the needle The drip is then begun at 5 drops per min and thereafter the rate of administration is slowed or increased until the desired response is obtained The relatively high concentration of oxytocin used reduces to a minimum the amount of saline given, and since there is no danger of thrombosis very slow drip rates are practicable The standard intravenous clip lacks sensitivity of control, and that recently described by Waller [2] has proved invaluable and greatly facilitates the initial regulation of the drip

The average case has required approximately 0 2 unit of oxytocin per hour, which is the same as by the intravenous route, and although the rapidity of response is slightly reduced this is not sufficient to influence either the control or safety of the method The hyaluronidase is effective for at least six hours, but it has been the custom to inject a further 1000 Benger units into the rubber tubing every four hours and ensures a constant rate of flow

The patient is allowed to sit up and is encouraged to herself usefully with knitting, neither of which is p with an intravenous needle

As with the intravenous route, continuous intra muscular oxytocin has been found particularly us in cases of failed surgical induction and hypoto inertia, and as a means of inducing labour with the not engaged in the pelvic brim It must be emphas that hypertonic uterine inertia associated with distress colicky pains and cervical achalasia, and major ceph pelvic disproportion are both an absolute contra indication to oxytocin therapy

Hyaluronidase in therapeutic doses is non toxic, a no adverse local reactions have been observed.

Guy's Hospital,
London, S E 1 J M HOLMES

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[1] Holmes J M *Lancet* 1954, ii, 1191
[2] Waller, R V *Ibid*, p 849

PEPTIC ULCERATION IN SOUTHERN NIGERIA

SIR,—I have read with great interest the lette relating to my paper (Nov 20) from Dr Buxton (Dec 11 Dr Watson Smith (Jan 1), and Mr Rose (Jan 8)

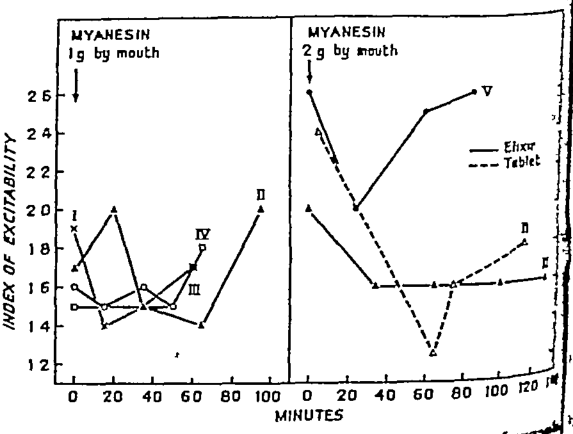
As to the psychosomatic aspect, other conditio thought to develop on this basis, such as thyrotoxicos coronary thrombosis, and ulcerative colitis, are qu uncommon in Southern Nigeria I agree that " the exa mation of physiological fluids is child's play compared wi the intricacies of the psychosomatic side " The poi however, is that though we all appreciate these intricac their study has not helped to solve the ulcer proble Peptic ulceration in Southern Nigeria is a distinct patho logical entity occurring in an area with well def climatic and agricultural features, and it may well that measuring physiological fluids and other substan will shed a little light on certain aspects of the probl

To Mr Rose I would reply that in Southern Nig heavy infestation with hæmatobium is not comm found, whereas infestation with other helminths, nota ascaris and to a lesser extent ankylostoma, is comm We have examined several specimens of duodenal ul to exclude hookworm as an ætiological factor, and such relationship could be established

University College,
Ibadan, Nigeria P G KONSTA

EFFECT OF MEPHENESIN ON MUSCLE EXCITABILITY

SIR—During a pilot study of neuromuscular exci bility in man (to be published) I noted an appar increase in excitability following therapeutic doses 'Myanesin' (mephenesin) Owing to certain pract difficulties this investigation was not completed, and I therefore prompted to record the initial results in t hope that others will confirm or disprove them



Changes in muscle excitability after oral administration of my

The excitability of the abductor pollicis brevis of five niversity students was measured with a Ritchie Sneath onstant voltage stimulator before and after the oral dministration of myanesin in 1 g and 2 g doses The onditions of the experiment were rigidly controlled (as ill be described elsewhere) The index of excitability dopted was the ratio between the minimal voltage equired to produce a contraction at 0 01 milli-sec ulse-length and the rheobase (i.e the smaller the index, he greater the excitability)

The accompanying figure shows that in all but one ase there was an increase in excitability shortly after ngestion of the myanesin.

Bromley Kent. DAVID M ZAUSMER.

CONGENITALLY SHORT FRENULA OF UPPER LIP AND TONGUE

SIR,—The gap between the permanent upper central ncisors, referred to by Mr Oldfield in his article of March 12, is of interest to dentists and orthodontists. Some years ago, the teaching was to remove the frenulum and perhaps some of the bone when these two teeth were separated There is abundant evidence in the form of serial models to show that it is normal for them to be separated at the time of eruption and that later they come ogether naturally but there are cases in which this does not occur

Radiographs disclose a difference in the appearance of the bone of the maxillary suture between these teeth In the normal case the suture terminates in two distinct Vs of compact bone, each enclosing cancellous bone In he other case the appearance is variable: the Vs are ot to be seen and the bone between the teeth appears o be cancellous, having a more or less square end. After emoval of the frenulum and perhaps some of the bone, n such cases and artificially bringing the teeth together elapse has followed removal of the appliance

The same bone condition may be seen in the deciduous entition, and I suspect this will be followed by permanent eparation of the upper permanent centrals

It is normal for deciduous centrals to be separated on ruption and during their life and for the attachment of he frenulum to migrate from a point near the alveolar dge to one higher in the sulcus there may be a very mall proportion of cases in which this does not occur nd in them it may be a factor in keeping the centrals part

London, W 1 HAROLD CHAPMAN

SIR,—The pendulum has swung rather far if it has led o the assertion that there is no such thing as a short renum Almost every speech defect has been ascribed o tongue tie even stammering but defects of rticulation are much more commonly due to hearing efects neuromuscular abnormalities emotional imma urity and lack of intelligence Even a glossectomised atient can speak intelligibly and speech can be normal n spite of short frena linguæ I have seen two young eople with this condition who were training for the tage and who were able to reach the required standard f clarity of diction Certainly there are such things as hort frena, but they are rarely the cause of speech efects

I have seen patients whose defective articulation was hought to be due to tongue tie a phonetic test showed they ere able to pronounce words with t d l n (the lingua-alveolar ounds) in fact they were using these sounds instead of k g nd ng in their dyslalic speech!

In 1935 I compared 180 children undergoing orthodontic reatment with 30 controls examined by the orthodontist and assed as having no dental irregularities and another 20 hosen at random. The aim was to ascertain the relationship etween faults of dentition and defective articulation I ound no significant correlation; but among the controls there as one girl with a short tongue frenum whose speech was normal and free even from minor errors found in others with normal frena and normal dentition.

Where short lingual frenum and high palatal arch are found together speech is more likely to be defective Intelligent, emotionally stable healthy people can over come a slight physical handicap without operation or speech therapy

London, N W 11 JOAN H VAN THAL.

TUBERCULOSIS IN IMMIGRANTS

SIR —We would like to reply to some further points raised by Dr James (April 9)

First that we believe without having carried out a single preliminary test that it is the tuberculin negative Irish who develop disease in England This bare state ment may reflect Dr James's interpretation of our point of view, but this is what we said

> 'From a third to a half of Irish immigrants aged 15–25 *from rural areas* are estimated to be non reactors to tuberculin. It is suspected that most of the Irish patients especially females, who later develop tuberculosis, are recruited from this group A smaller proportion break down as a result of progression or recrudescence of infection received before *leaving home*

So far as we are aware no evidence has yet been presented to refute this statement, on the contrary the report of the National Tuberculosis Survey in Ireland produces factual evidence which is entirely in keeping and Flynn and Joyce have suggested that we have underestimated the extent of the problem The conclusions reached in both publications were similar to our own

> The point regarding the lack of preliminary tuberculin tests was not in our power to rectify as the investigation was conducted on hospital patients already diagnosed we related our findings in those patients to those of other investigators whom we deem reliable, who had produced evidence regarding the high rate of tuberculin negativity in rural Ireland and we made deductions therefrom which appeared to us reasonable Even so we stated that the facts that we have collected are objective data but the interpretations we have made may not be correct and some are necessarily speculative; more evidence and much hard thinking are still required" We are prepared to accept legitimate correction of our viewpoint on evidence supported by facts, but polemical statements cannot be accepted as evidence

Secondly Dr James's statement that the idea that tuberculosis arrived here recently is quite fantastic it was recorded as a cause of death in Irish cities in the 17th century and I have no doubt it was known much earlier This crushing broadside merely indicates once more that Dr James has not made sure of his target before pulling the trigger Our statement reads: 'Ireland did not experience the *peak* of its epidemic wave until much later than England Ireland is now at a stage of development passed by England some considerable time ago and it is to this fact rather than to any racial' weakness in the Irish that the higher proportion of susceptibles is due We were also at some pains to point out that it was the *rural* Irish to whom our argument mainly applied and that migration of such susceptibles to cities where infection is much more likely to occur is important in the epidemiology of tuber culosis Dr James believes that those already infected are responsible for the high incidence in immigrants What does he think happens to the tuberculin negative? Do they stay at home successfully avoid infection after arriving in cities or invariably overcome it when it occurs? They must do one of these things if they do not provide the raw material for many of the cases we see

The point about the Irish famine and tuberculosis is a more serious one Disastrous and widespread as it was its effects cannot be considered identical with those of the sustained, centuries-old, endemic infection in cities

The Irish report recognises this when it indicates that the death rate increased again after an interval "when a new generation presented a sufficiency of pabulum" *Natural* resistance we believe is of fundamental importance in determining the course of tuberculous infection, even the point regarding Mantoux negativity or positivity on arrival in Britain is of lesser import, for the place where infection occurs has little bearing on the subsequent course of the disease

Dr James insists that "the intensity of infection in any country is the decisive factor in causing tuberculosis, and that the eradication of tuberculosis is not made easier by those who point out spurious short cuts upon which to waste energy and resources" If this mighty blow is intended for us we would refer him to the concluding sentence in our article "This suggestion [for B C G immunisation of immigrants before leaving home] does not imply any relaxation in other measures at present being applied to combat or prevent tuberculosis It is in no sense a substitute for good nutrition, improved housing, or adequate treatment of the infectious patient" We also proposed that "in addition to vaccination before the immigrants leave Ireland, a follow up would be desirable in this country to detect reverters, to re vaccinate where necessary, and to control the health of immigrants by routine radiography Effort, organisation, and coöperation would be required from authorities on both sides of the Irish Sea, but there is the prospect of a considerable alleviation of human suffering and misery, and probably of a considerable reduction in public-health expenditure, for tuberculosis is a costly disease"

We regard the supervision of the health of immigrants as vitally important It implies routine tuberculin testing in Ireland beforehand—a measure which in itself, according to the Irish report, leads to more efficient detection of the unknown sputum-positive person—and should help to discover potential sources of infection in Britain at an early stage, if this is a "spurious short-cut" it seems to us one which is remarkably difficult to accomplish

Regarding the efficacy of B C G vaccination in preventing pulmonary tuberculosis, we retain an open mind That it is a complete answer we do not claim, we do suggest it should be tried If Dr James disagrees we should be grateful if he would state his reasons

The whole subject of immigration and tuberculosis is beset with quite extraordinary difficulty, further investigation is important and *facts* are required If Dr James wishes to substantiate his statement that those already infected are responsible for the high incidence in immigrants, either by progression of the infection or by "reinfection," it would benefit his case enormously were he to produce evidence to this effect Until such evidence is forthcoming we must adhere to the point of view we now hold

Clare Hall Hospital,
Barnet

NORMAN MACDONALD
EVELYN V HESS

THE CLOUDED CRYSTAL BALL

SIR,—I cannot resist expressing my concern for poor old Whiddon's nephew (April 16, p 811), partly, of course, because I simply must do something with the leisure afforded me by our technical staff Since, no doubt, this young man holds Harry Hawke in the highest esteem, it is likely that he will come to believe earlier than usual in his career that there necessarily must be some irremediable taboo between bed and bench Later on, poor chap he may feel himself to be half a physician and indeed he might even become a specialist in diseases of the blood and then, oh dear, what confusion What is a hæmatologist ? Is he to be defined as a scientist who , a physician who a bleeder who ?

I do hope that Uncle Whiddon will convince his nephew that whether at bed, bench, or X ray table, he could still be a *doctor*

Upton, near Newark Notts

A B HILL

VACCINE LYMPH AND AUREOMYCIN

SIR,—The death of the Australian children received diphtheria-prophylactic supplied in large c tainers, referred to in your annotation of March 5, not due primarily to the large containers, as you sugg but to the fact that the material was supplied in co tainers holding more than one dose, *to which no antis had been added* The Therapeutic Substances Regulatio of 1931 and of 1952 require that "when any therapeuti substance is issued in liquid form in containers which are sealed in such a manner that portions of the contents can be withdrawn for use on different occasions, the liquid shall contain a sufficient proportion of some bacterio static to prevent the growth of any organism which may be introduced in the process of removing a portion of the contents of the container"

I think the distinction is important, because the use of multi dose containers is not objectionable, provided a effective bacteriostatic is present

Department of Bacteriology,
Wellcome Research Laboratories,
Beckenham Kent

A E FRANCIS

HARDENED FATS AND LUNG CANCER

SIR,—Dr Bender (Feb 12) has drawn attention to the content of essential fatty acids (E F.A) in samples of American margarine oils and butter

The reference to the paper in question[1] is not compl without mentioning that hydrogenated coconut-oil w found to contain no linoleic acid and no arachidonic acid and that bioassay methods showed that some margarine oils contained 2 4–6 8% linoleic acid and the much-used "selective" hydrogenated oils 0 9–3 0% linoleic acid. No of them contained arachidonic acid, and non winter cottonseed oil (not hydrogenated) contained 42–48% lino acid Long stability shortenings have great resistance to oxidation through virtual elimination of the polyunsatur fatty acids, including the E F.A Butter contains 3 2–4 linoleic acid and 0 2% arachidonic acid having a biopote 6 2 times that of linoleic acid when fed in mixture w linoleic acid to fat-deficient rats[2] As to "selective" hyd genation, the aim is not to saturate all double bonds of fat but to be satisfied with the conversion of linoleic acid linolenic acid to oleic acid How well this destruction of E.F can be completed is clearly demonstrated

In the United States margarine changed during the 191 period from a product manufactured mainly from ani fats to one in which coconut oil, and later cottonseed and soybean oil, predominated The American marga and shortening industry has therefore had to depend more more on the E.F.A reducing hydrogenation processes Ameri margarine can be made without or with some linoleic a but does not contain the valuable arachidonic acid. can therefore easily be responsible for low dietary intake E.F A.

In the United Kingdom in 1946 cottonseed and soyb oil were very scarce, coconut, groundnut, palm kernel, marine oils were the main raw materials The risk of a E F.A diet is thus possible

An idea of the human requirement of E F.A can be obta from the fact that human milk fat contains 9 1% E.F. representing 13 3 per 2500 calories of the milk For ad the requirement will be less

Food consumed domestically in the U.K (1952) cont about 3 5 g linoleic acid per 2500 calories, equal to 3 4 g p head per day An estimate based on Drummond's[4] midd class diet (1939) gives 4 2 g per 2500 calories and 5 5 g p head per day If these diets are representative the aver consumption of linoleic acid fell between 1930 and 19 from about 5 to 3 g per head per day The consumption arachidonic acid fell at the same time from 0 8 to 0 3 g

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1 Deuel, H J jun Greenberg S M, Anisfeld L, Melnick, J Nutr 1951 45 535
2 Greenberg S M Calbert, C E, Deuel, H J jun, Brown, *Ibid* p 521
3 Standard Values in Nutrition and Metabolism Edited E C Albriton Philadelphia 1954 p 111
4 Drummond J C Wilbraham A The Englishman's Fo London 1939, p 565

With a decrease in an already low E.F.A. diet the risk that more and more people receive less than their optimal requirements will grow considerably. (The present incidence of lung cancer requires only that the lungs of less than 1% of the population are rendered more vulnerable to cancer-producing substances by a defect in a defence mechanism.)

10 g. more lard would increase the intake of linoleic acid by more than 0·8 g.; and of arachidonic acid by about 0·1 g. 10 g. olive-oil gives 0·8 g., 10 g. groundnut-oil 2 g., and 10 g. corn-oil 4 g. linoleic acid. People living in regions where, for instance, the diet is rich in lard (pork) or olive or groundnut or corn oil (whole corn) will thus easily receive a diet rich in E.F.A., even on a low-fat diet, which can also be an advantage. Overweight individuals are more liable to develop cancer than average or underweight, and long-term caloric restriction tends to suppress tumour formation in mice.[3]

Your annotation of Feb. 19 on cancer clues, Professor Banks's letter of March 5, and the differences in incidence of lung cancer between different regions where the diet may easily vary in E.F.A. content strengthen the view that other ætiological factors than smoking should be investigated.

Copenhagen. JOHAN E. NYROP

POSTOPERATIVE MEMBRANOUS TRACHEOBRONCHITIS

SIR,—We were much interested in the article by Mr. Dark and Mr. Jewsbury in your issue of Feb. 26, for we have recently seen a case which, we think, is very similar to those they describe.

A man of 19 attempted to commit suicide by taking a barbiturate. He came into hospital deeply comatose, and bronchoscopy was performed because he had aspirated vomit. After bronchoscopy breathing was still laboured and a no. 9 cuffed Magill tube was passed and left in place for about eighteen hours.

Three days later, after the patient had recovered consciousness, he noticed in his sputum a membranous cylinder about 5 cm. long and moulded perfectly by the trachea. The patient recovered and a further bronchoscopy was not thought necessary.

Microscopic examination of the cylinder showed clotted blood, fibrinous material, and polymorphs, with no evidence of mucosal elements—findings similar to those reported by Mr. Dark and Mr. Jewsbury.

1st Surgical Clinic and 2nd Medical Clinic, Hospital Escolar de St. Marta, Lisbon. ANTONIO COITO ANGELO FLORA

HYPOTENSION TREATED WITH CONTINUOUS NORADRENALINE

SIR,—The following case may be of interest to your readers.

A healthy active old man of 89 fell and broke his leg on Sept. 29. X-ray examination revealed a subtrochanteric fracture of the left femur with moderate displacement. His leg was put up on skeletal traction and a Thomas's splint. His general condition was good.

On Nov. 13 there was no evidence of callus at the fracture site, and on Nov. 19 an open reduction with plating of the femur was performed under general anæsthesia. About a pint of blood was lost, and during the operation the patient became very shocked with, at times, an almost unrecordable blood-pressure. 3 pints of blood was given in the theatre. Five hours later the systolic pressure was 70 mm. Hg and could not be raised by any of the usual anti-shock methods. The patient was still unconscious.

Eight hours after the operation an intravenous drip of normal saline solution containing *l*-noradrenaline (‘Levophed’, 4 mg. per litre) was started at the rate of 2 ml. per min. Within five minutes the blood-pressure was 100/100 and the patient had regained consciousness. The blood-pressure was maintained at 130/90 by running the drip at about 1·5 ml. per min.

During the next sixty hours it became possible to slow down the drip, but on completely stopping it the systolic pressure fell to 70 or less, and it was not until the end of this time that the patient became able to maintain his blood-pressure at 130/80 by normal reflex mechanisms.

He subsequently recovered to a very large extent, eating and drinking normally, but extensive sacral sores developed under the plaster spica, and the resulting toxæmia led to his death on Dec. 25.

The severe and persistent hypotension was probably due to adrenal exhaustion. In view of the relatively high cost and scarcity of adrenal cortical extracts, *l*-noradrenaline seems to be a useful substitute in some circumstances.

My thanks are due to Mr. N. Ross Smith and Dr. R. D. Scott for permission to publish this case.

Boscombe, Hants. M. V. GUILMANT

THE HAIR OF THE PILONIDAL SINUS

SIR,—I know of two apparently typical ‘pilonidal’ sinuses in the natal cleft which contained instead of hair pieces of grass. In these interesting cases the sinuses were originally lined with turf. The turf, having shed the piece of grass, was then destroyed by granulation tissue so that it was not found in the operation specimen; but one knows that turf must have been there originally by analogy with the much more common hair-containing sinuses which are originally lined with hair-bearing skin.

Or perhaps Mr. Weale (*Lancet*, April 16) and the endogenists are wrong, and the reason why one does not find a grass-bearing (or hair-bearing) lining is that there never was one and the grass (or hair) gets in from the outside.

London, W.1. B. H. PAGE

PITUITARY STIMULATION OF ERYTHROBLASTIC MITOSES IN BONE-MARROW

SIR,—In the course of investigations into the influence of the pituitary on erythropoiesis we have found that the pituitary plays an important part in erythroblastic mitoses in bone-marrow.

The reproductive activity of the myeloid cells has been estimated by the stathmokinetic test, using colchicine. It is well known that, in any type of tissue, the number of mitoses blocked by colchicine in a certain time is related to the proliferative activity of the cells.

Using this technique 10 normal rats were injected with colchicine (1·75 mg. per kg.). Nine hours later 71·1%±14·8% of the basophilic erythroblasts, and 56·8%±12·8% of the polychromatophilic erythroblasts in the bone-marrow were in mitosis (stathmokinesis). On the other hand fewer granuloblastic mitoses were blocked: 31·4%±0·3% in myeloblasts and 2·8%±1·5% in myelocytes.

In 10 hypophysectomised rats, of the same strain, age, and sex, ten days after the hypophysectomy, the colchicine blocked 26·2%±13·1% mitoses in 100 basophilic erythroblasts, and 15·8%±14·6% mitoses in 100 polychromatophilic erythroblasts. But no great difference was found between the proportion of mitoses blocked in the granuloblasts of the hypophysectomised and of the normal rats.

The reduction of the reproductive power of erythroblasts after hypophysectomy is followed by the well-known reduction of reticulocytes in bone-marrow and in blood, by intense medullary erythroblastic hypoplasia, and later by anæmia.

Hypophysectomy, however, does not modify the mitotic rhythm of granuloblasts and *does not reduce the granuloblastic quota of the bone-marrow*. Therefore *the so-called pituitary regulation of erythropoiesis seems to be based on a regular and selective pituitary stimulation of the mitotic rhythm of the medullary erythroblasts.*

Medical Clinic, University of Pavia, Italy. GIUSEPPE MARI[illegible] FRANCESCO [illegible]

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[3] Tannenbaum, A. Approaches to Tumor Chemotherapy. Washington, 1947; p. 101.

Obituary

EVELYN CHARLES SPRAWSON

M C, D Sc, Lond, M R C S, F D S

As professor of dental surgery and pathology at the London Hospital, and as chairman of the board of studies in dentistry of the University of London, Evelyn Sprawson was one of those who did most to raise the general level of dental education and research in this country

Born in 1881, he was educated at King's College School, London, and began his dental studies at the Royal Dental Hospital, where he won the Walker and Saunders scholarships After taking the L D S in 1902, he continued his medical studies at Charing Cross Hospital and gained the Conjoint qualification in 1905 Having set up in practice in Cavendish Square, he joined the staff of the City of London Hospital for Diseases of the Chest, and became assistant dental surgeon and lecturer in histology at the National Dental Hospital When the London Hospital Dental School was formed in 1911 he joined the honorary staff But his work there was interrupted by the outbreak of war He served as a captain in the R A M C and was mentioned in despatches and awarded the Military Cross for his gallantry in action

On his return in 1919 he retired from private practice and was appointed the first director of dental studies at the London Hospital Thenceforward he gave all his time to teaching and research, and he published papers on a wide range of subjects in dental histology and pathology, including his important studies on dental enamel, odontomes, abnormalities in dental structure, and the effect of diet on tooth formation His work at Dr Barnardo's Homes, to which he was dental surgeon from 1908 to 1953, gave him unusual opportunities for controlled clinical observation F N D recalls that

> "the first result of these studies was his papers on the percentage of organic matter in human tooth enamel, for this thesis based on this investigation, he was awarded the degree of D SC by the University of London He then turned his attention to the relative effects of raw and pasteurised milk in promoting adequate calcification in teeth, he believed that raw milk contained an activating agent which was inhibited in pasteurised milk The statistics which he based on his continual observations of children in Barnardo's Homes were carefully prepared and deserve more consideration than they have yet received "

He received the Tomes prize of the Royal College of Surgeons for 1927–29 and was awarded a Hunterian professorship in 1936–37 He was associated with the late Sir Frank Colyer in the revision of several editions of *Dental Surgery and Pathology*, and "Colyer and Sprawson" remained for years the standard textbook on the subject He also edited the *British Dental Annual* in 1952

In 1940 Sprawson was appointed to the chair of dental surgery at the London Hospital He examined for the Universities of London, Birmingham, Durham, New Zealand, and Witwatersrand, for the Dental Board, and for the Royal College of Surgeons of England He was among the first to be elected to the college's fellowship in dental surgery, when this was started in 1947 In the same year he delivered the Charles Tomes lecture to the college As well as being chairman of the University Board of Studies in Dentistry, he was deputy chairman of the Dental Education Advisory Committee, and a vice-president of the International Association for Dental Research His work for these bodies reflected his interest in his specialty and in education, but he also offered his medical colleagues able and devoted service through the Medical Protection Society, of whose council he was a member for nearly 17 years "His quiet manner," E R C writes, "covered a shrewd and determined character his advice on medicolegal problems was invaluable" To another fellow member of the council he admitted that, of all the bodies on which he served, the meetings of the Medical Protection Society were those he most enjoyed He died at a meeting of the council on April 6, at work among his friends

To Sprawson, the man and colleague, F B B pays the following tribute

"Modest, unassuming, and gentle, and very much on the quiet side, Sprawson never spoke much about himself but always with great intensity about anything on which he was engaged, or which might be the subject of discussion or conversation He had many admirable characteristics, but to my mind the one that was most outstanding was the thoroughness with which he dealt with anything he undertook A notable example of this was an occasion when he had to give expert evidence for the defence in a case in which the mandible had been fractured during the extraction of a molar tooth. Realising that it might be difficult for the Judge to understand the technicalities of the case by mere verbal explanation, he took with him to the court a mandible and specimens of the instruments used When giving his evidence at the hearing, he produced them, and this so pleased the Judge that he invited Sprawson to the Bench, where he gave a first-rate demonstration of the operation He was keenly interested in numismatics, chiefly the coinage of the Hanoverian period, and he was often to be seen at Glendining's sales He was also a great gardener, and rarely missed the Horticultural Society's shows at Chelsea and Westminster It will be seen that he tended towards the quieter interests of life and apart from a little sporadic firing of a rifle, I never knew him to evince any interest in sport, outdoor or indoor of any kind Essentially studious, he always seemed happiest when attempting to elucidate some scientific problem. He was a lover of books, especially of biographies and of works on dental surgery, whether ancient or modern

"He had a quiet voice, and a somewhat halting delivery, and he often asked me whether he spoke loudly enough when talking at a meeting, and told me that being partially deaf, he could not gauge the power of his voice But, somehow, I always thought that his quiet voice was all a part of the gentleness of the man, and gentle he was, I never saw him angry, sometimes indignant at the obviously wrong perhaps but *never angry* "

But it is perhaps as a teacher that Sprawson will be rememberd, and the last word must lie with those he taught

"We at the London,' writes S G A, "have very affectionate memories of Sprawson, tall and spare, striding along in a cloud of tobacco smoke, or lecturing in his room in his soft hesitant voice, his words carefully chosen and his subject matter enlivened with interesting reminiscences and literary quotations His kindness and consideration endeared him to all his students and it was a memorable evening in 1947 when a gathering of past and present members of the London Hospital Dental Society presented him with a portrait and announced the institution of the Evelyn Sprawson prize on the occasion of his retirement from the hospital When the final assessment is made it may well be decided that his chief claim to fame was not in his scientific contributions to dentistry but in his success as a teacher, for he who could instil and maintain such a feeling of affection and gratitude in the hearts of all his students must surely have been in possession of a rare gift"

Appointments

DALY N A, M.B Belf, D.P M asst psychiatrist (S H.M.O.) Littlemore Hospital Oxford

RITCHIE F A A M B Lond M R C P D P M senior asst psychiatrist, Rauceby Hospital Sleaford

Leeds Regional Hospital Board

HANSELL, J L M B Camb asst chest physician and deputy medical superintendent (S H.M O), The Hospital, Grassington near Skipton

PRATT T L C M R.C.S D M R.D asst radiologist (S.H.M.O.) Huddersfield and Halifax groups

WHITE J M, M D Glasg D I M consultant psychiatrist and deputy physician-superintendent Stanley Royd Hospital Wakefield

Appointed Factory Doctors

EVANS D M L M B Lond Newport Pembrokeshire

FRISKNEY C E, M B Edin Spilsby Lincs

GREEN G I M B Camb D M R.T Batley, Yorks

HILL, R D M B Aberd Nesting (No 2) Shetland

MACLEOD R C M B Glasg Strachur Argyllshire

PARR R. T M B Durh, D OBST Broughton Hants

SCOTT H G M B Dubl Market Rasen, Lincs

SCUDAMORE T O M B Camb, D OBST Stapleford Notts

TYTLER PETER M B Aberd Unst, Shetland

WIGGLESWORTH, G F M B Lond Howden Yorks

Notes and News

CUT IN DENTISTS' PAY TO END

On March 17 the Minister of Health notified the British Dental Association[1] that he was prepared to abolish the 10% cut in dentists' pay imposed in 1950.[2] He was not satisfied that on purely statistical evidence a case for restoration had been made but in view of the whole position he was willing to end the cut subject to the following conditions:

1. That "the re-assessment of dental remuneration and the recasting of the scale of fees should be dealt with together."
2. That "this should be accepted as a full settlement of dental remuneration at the present time."

The Minister has in mind that the new scale, which is to be drawn up in consultation with the association, should give dentists the net incomes that they would have received in 1952–53 had the 10% reduction not been in effect. While the new scale is being worked out the Minister is willing to cancel the 10% reduction.

On March 31 the remuneration subcommittee of the General Dental Services Committee recommended the rejection of the Minister's offer, mainly on the ground that it would mean giving up for ever the Spens Committee's recommendations and the association's claim, based on them, for a scale which would produce an average net income of £2200. But after consideration the G.D.S. Committee decided not to accept the subcommittee's views but to advise the Representative Board to accept the Minister's offer. The board was impressed by "the danger of refusing something palpable and embarking again on an interminable series of negotiations" and after a full discussion agreed to accept the Minister's proposals.

SCOTTISH REGIONAL HOSPITAL BOARDS

The following doctors have been appointed to the hospital boards. New appointments are indicated with an asterisk.

Northern Regional Hospital Board.—C. B. MacLeod, L. M. V. Mitchell.

North Eastern Regional Hospital Board.—Lady Taylor, H. Gordon Smith.

Eastern Regional Hospital Board.—J. Gordon Clark, A. F. Wood.

South Eastern Regional Hospital Board.—Prof. D. M. Dunlop, T. McWalter Millar.

Western Regional Hospital Board.—Prof. G. M. Wishart, E. G. Butler, D. Livingston Kerr.

SALE OF HORMONES

The council of the Pharmaceutical Society of Great Britain is advising pharmacists not to supply sex hormones or preparations containing them unless they are satisfied that customers are obtaining them on medical advice, though not necessarily presenting a prescription. No decision has yet been reached about cosmetic preparations containing hormones.

IDIOPATHIC THROMBOCYTOPENIC PURPURA

In our recent leading article[3] we referred to a report by Tullis[4] that serum from some patients with idiopathic thrombocytopenic purpura caused agglutination and even lysis of normal platelets in the presence of complement. In an earlier report[5] Dausset et al. in Paris had recorded a similar finding: the serum of a patient with acute idiopathic thrombocytopenic purpura caused rapid agglutination followed by destruction of normal platelets in vitro and inhibition, in the presence of calcium, of clot retraction of normal blood or of recalcified citrated plasma.

A HANDMAID OF MEDICINE

The Medical Artists' Association of Great Britain has gathered together in an exhibition called Art in the Service of Medicine, and held at British Medical Association House, Tavistock Square, W.C.1, an imposing array of drawings intended to illustrate the training and scope of medical artists. Most of the exhibits are drawings or paintings of medical subjects, but there are also wax models and castings in plastic resin of bronchial trees and cerebral ventricles. As works of art for pathological museums and the walls of dissecting rooms the exhibits are excellent, but insufficient emphasis is laid on the preparation of drawings and paintings for illustrating published articles. The requirements of blockmakers and printers are neglected except for one original painting set by the side of the final reduction in print and another original painting set alongside the different stages of its reproduction by seven-colour offset lithography. These two exhibits illustrate the way in which the blockmakers and printers deal with the artists' material rather than the way in which the artists meet their requirements. In this wealth of beautiful drawings there is but one chart, and that depends on colour to distinguish between the curves. These last two items are far from practical. It is to be hoped that a similar exhibition will become an annual affair at which much more attention will be paid to charts, diagrams, and other illustrations intended for reproduction in medical books and journals.

SOCIAL MEDICINE IN THE SOUTH SEAS

There are no half measures about the South Sea Islands. They either bring out the worst or the best in people. In Dr. Davis and his wife they have brought out the best, as is shown by their joint account of his foray into social medicine.[1] Of Welsh and Polynesian descent, he was born in the Cook Islands, graduated in medicine in New Zealand during the war, and returned to the Cook Islands with his wife, a New Zealander, to lead a campaign for the improvement of health and living conditions which had been disrupted by the falling economy of the war years. The story of this campaign, with his triumphs and disappointments, his battles against the administration, and his efforts to gain the confidence of the islanders, is delightfully and modestly unfolded. He set about his task with the zeal of a missionary, and he was well armed with his knowledge of and sympathy with the islanders' point of view. He fought the old prejudice against modern medicine, yet was able to gain the support of the witch doctors, who despite laws passed against them still flourished. In the teeth of opposition he sided with the islanders in their efforts to secure a greater share in administration of the islands and in repelling the Communist infiltration which had been encouraged by the economic depression. The final chapters tell of a voyage in a tiny sailing ship which Dr. and Mrs. Davis, with their two small sons and a crew of two, made in mid winter across the Pacific to South America and ultimately to the United States.

This story of high courage and adventure, told with simple sincerity and quiet wit, will delight those who like to hear about solid achievements in social medicine, and also those of us who, like Tartarin de Tarascon, dream of stirring deeds but are too timid to cross the bridge over the river.

University of Oxford

Dr. G. W. Pickering, who holds a chair of medicine in the University of London at St. Mary's Hospital Medical School, has been appointed regius professor of medicine. He will take up his appointment next year when the laboratory and unit of 25–30 beds now being built at the Radcliffe Infirmary for his department will be completed. Professor Pickering is to be the first regius professor of medicine to occupy the house in Norham Gardens which Osler bequeathed to the university.

Dr. Pickering, who is 50 years of age, was educated at the Royal Grammar School, Newcastle upon Tyne, at Dulwich College, and at Pembroke College, Cambridge, where he was a scholar. He obtained a first-class in both parts of the natural sciences tripos and in 1926 went to St. Thomas's Hospital. While working as a student he taught biology at Westminster School. In 1928 he qualified, and in the following year he was awarded the Mead medal and Wainwright prize for medicine at the hospital. He was resident anæsthetist and house-physician, and in 1930 graduated M.B. Camb. and became M.R.C.P. From St. Thomas's he went to University College Hospital as assistant in the department of clinical research under Sir Thomas Lewis, F.R.S. In 1931 he was appointed to the permanent scientific staff of the Medical Research Council. In 1932 he presented with W. Hess a preliminary account of his work on the experimental production of headache. This was followed by many other reports, especially on experimental hypertension and allied problems, and in 1936 he became lecturer in cardiovascular pathology. In 1938 he was appointed Herzstein lecturer in the University of California and Stanford University, San Francisco, and spent two months visiting these and other schools in the United States. He was elected F.R.C.P. in 1938. The following year he took up his present chair at St. Mary's. In 1949 he visited Australia, New Zealand, and Africa as a Sims travelling professor. He has been a member of the University Grants Committee (1944–54), and was last year appointed to the Medical Research Council and the Clinical Research Board.

University of Durham

On Thursday, May 19, at 5 P.M., a memorial plaque to the late Professor Grey Turner will be unveiled in the Royal Victoria Infirmary, Newcastle upon Tyne. Afterwards Sir Zachary Cope will deliver the first Grey Turner lecture. He is to speak on Some Early Medical Museums.

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[1] Brit. dent. J. April 5, 1955, p. 261.
[2] See Lancet, 1950, i, 822.
[3] Lancet, March 5, 1955, p. 491.
[4] Tullis, J. L. New Engl. J. Med. 1953, 249, 591.
[5] Dausset, J., Delafontaine, P., Fleuriot, Y. Sang, 1952, 23, 373.

[1] Doctor To The Islands. By Tom and Lydia Davis. London: Michael Joseph. 1955. Pp. 287. 15s.

University of Edinburgh

Dr Douglas Guthrie during the summer term will give six lecture demonstrations surveying early medicine At the first lecture on May 2, at 5 P M, at University New Buildings, Teviot Place, he will speak on Magic, Witchcraft, and Medicine

Royal College of Physicians of London

On Tuesday and Thursday, May 3 and 5, at 5 P.M, at the college, Pall Mall East, S W 1, Sir Horace Evans will give the Croonian lectures on the Significance of Certain Symptoms and Signs in Disease of the Kidneys

Royal College of Physicians of Ireland

On April 1 the following were admitted to the licence of medicine and midwifery of the college

Cassam Mahomed Bahemia, M J Doyle, Jalejar Burjorji Fanibunda, M H Heller, J S P MacGill, Cecilia M. McMorrow, B M. Rosovske, Muriel M. Tynan

Royal Institution of Great Britain

On Friday, May 20, at 9 P M, at the Institution, 21, Albemarle Street, London, W 1, Sir Wilfrid Le Gros Clark, F.R.S, will give a discourse on the Exposure of the Piltdown Forgery

Institute of Dermatology, London

A semipermanent exhibition by Dr L Forman, on Cutaneous Reactions Associated with Visceral Malignancy, will be open from May 5 to 25

Israel Medical Association

The third world assembly of this association will be held in Israel from Aug 10 to 20, with sessions at Jerusalem, Haifa, and Tel Aviv Further details may be had from Dr H Farkas, Embassy of Israel, 2, Palace Green, London, W 8

Medical Women's Federation

Psychological Medicine Group —At a meeting of this group, to be held on Friday, May 6, at 2 45 P M, at the Cassel Hospital, Ham Common, Richmond, Surrey, Dr T F Main will speak on Emotional Disturbance at Adolescence

St Mary's Hospital, London

Dr A. C Corcoran, medical director of the research division of the Cleveland Clinic, will give a lecture in the medical school at 5 P.M on May 24, on the Evaluation of Antihypertensive Drugs

Naval Medical Compassionate Fund

A meeting of the subscribers of this fund will be held at 3 P M on May 13, at the Medical Department of the Navy, Queen Anne's Mansions, St James's Park, London, S W 1, to elect six directors of the fund

Hunterian Society

The gold medal of this society for 1954 has been awarded to Dr Philip Hopkins The subject for the 1955 essay is Headache The competition is open to all general practitioners, and further details may be had from the hon secretary, Mr R S Murley, 95, Harley Street, London, W 1

Faculty of Homœopathy

At Hahnemann's 200th birthday celebration, to be held at 1, Wimpole Street, London, W 1, at 3 P M on Thursday, May 5, Dr F H. Bodman will speak on Hahnemann and his Patients, and Dr T Douglas Ross on Homœopathy's Heritage and Outlook Today Tickets may be had from the assistant secretary of the faculty, Royal London Homœopathic Hospital, Great Ormond Street, W C 1

Wright-Fleming Institute of Microbiology

Sir Zachary Cope will give the first of six Almroth Wright lectures at St Mary's Hospital Medical School, Paddington, W 2, on Tuesday, May 3, at 5 P.M He will speak on Peculiarities of the Clinical Pathology of Actinomyces The other lecturers are Dr D A Long (Response of the Host to Bacterial Infection), Mr A. T R Mattick, PH.D (Lactobacilli and some Streptococci), Lord Stamp (Action of Bacterial Enzymes on Immunising Antigens), Prof A C Frazer (Intestinal Function in Man), Prof B Ephrussi (Paris) (Intrinsic Factors Controlling the Synthesis of Cytochromes in Yeast) The lectures are open to all doctors and medical [illegible]

Society of Chiropodists

The annual dinner of this society will be held at Park Lane Hotel, Piccadilly, London, W 1, on F May 13

Worshipful Company of Barbers of London

At a meeting of the court of the Barbers' Company held a Tallow Chandlers' Hall on April 5, Sir Cecil Wakeley, Master, admitted Sir James Paterson Ross as an freeman

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The National Smoke Abatement Society has moved to [illegible] Chambers, Bridge Street, London, S W 1

Diary of the Week

APRIL 24 TO 30

Monday, 25th

ROYAL SOCIETY OF MEDICINE 1, Wimpole Street W 1
8 P.M *Pathology* Prof René J Dubos (New York) Effect of Metabolic Factors on the Infectious Process

MEDICAL SOCIETY OF LONDON, 11, Chandos Street, W 1
8 30 P.M. Dr J G Scadding Treatment of Pulmonary Tub culosis (Second Lettsomian lecture)

HUNTERIAN SOCIETY
8 30 P M (Talbot Restaurant, London Wall, E C 2) Pr E N de C Andrade, F R.S Isotopes

MANCHESTER MEDICAL SOCIETY
9 P M (Medical School) *General Practice* Dr Edmund Phill Aspects of General Practice

Tuesday, 26th

ROYAL COLLEGE OF SURGEONS OF ENGLAND, Lincoln's Inn Fiel W C 2
3 45 P M Prof R. J Last Form and Structure of Musc (Arnott demonstration)

ROYAL SOCIETY OF MEDICINE
8 P.M *Medicine* Prof E E Pochin Prof D W Smith Mr Norman Veall Radioactive Isotopes

Wednesday, 27th

MEDICAL SOCIETY OF LONDON
8 30 P.M Dr Scadding Treatment of Pulmonary Tuberculosi (Last Lettsomian lecture)

LONDON ASSOCIATION OF THE MEDICAL WOMEN'S FEDERATIO
8 30 P M (Royal Free Hospital School of Medicine, 8 Hunt Street, W C 1) Dr Dorothy Parkin Dr Helen Payli Wright, Miss Josephine Barnes Obstetric Problems General Practice

Thursday, 28th

ROYAL COLLEGE OF SURGEONS OF ENGLAND
5 P M Dr W T Cooke Nutritional and Metabolic Factors in th Ætiology and Treatment of Regional Ileitis (Hunte lecture)

UNIVERSITY OF LONDON
5 30 P M (London School of Hygiene and Tropical Medici Keppel Street W C 1) Professor Dubos Micro Envir ment of Inflammation or Metchnikoff Revisited

LONDON JEWISH HOSPITAL MEDICAL SOCIETY
8 30 P.M (11 Chandos Street, W 1) Dr I R. Marre Comm Skin Diseases

NUFFIELD ORTHOPÆDIC CENTRE Wingfield Morris Orthop Hospital Oxford
8 30 P M Mr R G Taylor The Brown Séquard Syndro following Trauma

HONYMAN GILLESPIE LECTURE
5 P M (University New Buildings, Teviot Place Edinbur Prof G J Romanes Motor Cells of the Spinal Cord

UNIVERSITY OF ST ANDREWS
5 P.M (Medical School, Small's Wynd, Dundee) Dr W Feldber F R.S A New Experimental Approach to the Pharmac logy of the Central Nervous System

Friday, 29th

UNIVERSITY COLLEGE Gower Street, W C 1
5 15 P M Dr S E Dicker Renal Clearances in Mammalia Kidneys (First of ten Cushny lectures)

ST MARY'S HOSPITAL MEDICAL SCHOOL, Paddington, W 2
5 P M Mr Ian Jackson Ectopic Gestation

INSTITUTE OF LARYNGOLOGY AND OTOLOGY, 330, Gray's Inn Ro W C 1
3 30 P M Mr J C Ballantyne Use of Hearing aids

UNIVERSITY OF OXFORD
NOON (Sir William Dunn School of Pathology) Professor Dubo Fate of Infectious Agents in vivo

Births, Marriages, and Deaths

BIRTHS

CLARKE —*On April 14, at Gosforth to Catherine wife of M* Patrick Clarke F R C.S —a son

TURNER WARWICK.—On March 25, to Margaret (née Harvey Moore) M R.C P, wife of Richard Trevor Turner Warwick, F.R.C. M R.C P—a sister for Gillian (Lynne Frances)

OSTEOPOROSIS*

A M. COOKE
D.M. Oxfd F.R C P
PHYSICIAN TO THE RADCLIFFE INFIRMARY OXFORD

THE SKELETON, out of sight and often out of mind a formidable mass of tissue occupying about 9% of e body by bulk and no less than 17% by weight As apper (1952) has cruelly said, When budding ysicians are first introduced to osteology, the skeleton ems to be only a collection of oddly shaped tubes and ates consisting of calcium carbonate and calcium osphate and most members of the medical profession erish this first impression for the rest of their lives' he stability and immutability of dry bones and their istence for centuries, and even millions of years, ter the soft tissues have turned to dust give us a false ea of bone during life Its fixity after death is in sharp ntrast to its ceaseless activity in life Bone is in fact e of the most plastic tissues in the body with a large etabolic *turnover, and ceaseless chemical and physio*gical activity throughout life It is a living tissue with ood vessels, nerves, and lymphatics

The Structure of Bone

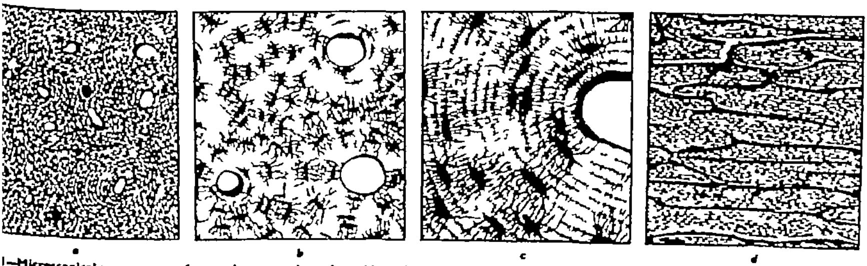
The gross anatomy of bone is too well known to quire more than passing comment The compact bone best seen in the shafts of the long bones The cancellous ne fills the ends of the long bones and the centra of the rtebræ and forms the greater bulk of small bones e anatomist s division of bones into the somatic and eral skeletons need not concern us here nor need we more than note in passing the division of the skeleton o cartilage bones and membrane bones The latter sification is of interest and importance from the int of view of development but once bone is formed, hatever the method of ossification its structure and ysiological behaviour are the same

n compact bone (fig 1) sections show the cylindrical versian systems consisting of a Haversian canal ntaining blood vessels and sometimes lymphatics rounded by concentric lamellæ (Havers 1691) The es between adjacent Haversian systems are occupied irregularly disposed interstitial lamellæ On the side, for example of the shaft of an adult long bone, the outer circumferential lamellæ which give a ooth surface to the bone and similarly on the inside e inner circumferential lamellæ. The general direction he Haversian canals is longitudinal, although they are united by oblique branching canals There are also canals at right angles to the bone surface by which nutrient vessels enter from the periosteum and communicate with the Haversian canals These are known as Volkmann s canals and were originally thought to be caused by blood vessels burrowing into the bone This is now known to be an incorrect view because all blood vessels in bone are developed in the matrix before ossification occurs. These canals are still known somewhat undeservedly by Volkmann s name

Cancellous bone consists of trabeculæ arranged either in a random three-dimensional lattice or condensed into so called lines of force" or trajectories Actually compact and cancellous bone are essentially the same in structure Both contain laminæ, and cancellous bone may contain Haversian systems They differ only in their spatial arrangement Every bone surface other than those forming joints is covered by a membrane on the outside inside the medullary canal, and over the surface of every trabecula This membrane is of course, known as the periosteum on the outside of the bone and the endosteum on the inside, but its function is precisely the same in both situations The bone membrane contains osteogenic cells and plays a vital part in bone growth

This is no place to enter into the interesting controversy about the function of the periosteum that has raged for two hundred years Equally competent and careful workers have performed the same experiments and obtained exactly opposite answers—on the one hand that the periosteum can produce bone *de novo* and on the other that its function is to limit and restrict the growth of bone Indeed, Sir Arthur Keith was forced to conclude that it looked as though the dogs of Edinburgh and Lyons were provided with a different kind of periosteum from the dogs of Glasgow The explanation is now thought to be that the naked eye periosteum is different from the microscopic periosteum The former has two layers, an outer and obvious connective tissue layer and an inner and scarcely visible layer containing osteogenic cells When periosteum is stripped from bone, the outer layer is removed but part of the inner layer with its osteogenetic possibilities remains adherent to the *bone and part to the main sheet* of periosteum (Ham 1934) This proves both sides of the controversy to have been right but has made the papers of modern authors on bone growth rather less exciting

The shape of a bone is determined by various factors. The first is an intrinsic growth pattern presumably related to the presence of organisers Murray and Huxley (1925) Willis (1936) and others have shown that a tissue-culture of the axial mesoderm of a limb bud will show a surprising degree of anatomical development In the case of the lower limb the tissue-culture differenti



1—Microscopical appearances of normal compact bone from Hassall (1849) a b and c are low medium and high-power transverse sections and d a low-power longitudinal section ates into a recognisable femur, with head, neck, trochanters, and condyles, and may even show the beginnings of joint formation Secondly, the shape of a bone is modified by the mechanical forces that the bone is there to resist Numerous observations have shown that if by accident in man, or by experiment in animals, a limb is deformed or one of the bones in the forearm removed, all the bones in the limb will rapidly adapt themselves to the new functional requirements This phenomenon is related to the disposition of the trabeculæ and the formation of trajectories, about which I shall have more to say shortly Thirdly, some bones are modified by the soft organs which they enclose—the skull by the brain, the ribs by the lungs, and the otic, optic, and nasal capsules by their contents Fourthly, bones must compromise with neighbouring organs, as shown in the human tibia which is moulded by lateral pressure of the muscles lying against it Fifthly, the shape of a bone may be influenced by the earlier structures that it has superseded, such as the relation of early cancellous bone to its preceding cartilage The last factor is respect for the needs of the other functions of bone—for example, leaving room for the marrow (Murray 1936)

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*ridged from the Lumleian lectures for 1955 delivered before the Royal College of Physicians of London on April 10 and 21 under the title of Some Aspects of Skeletal Disease

Bone under Stress

Of these factors, one which I should like to deal with in greater detail because it is relevant to my general theme is the second—namely the effect of stresses and strains on bone This is a problem that has exercised anatomists, zoologists, and physiologists for over a century As long ago as 1827 Sir Charles Bell wrote that "This minute lattice work, or the cancelli which constituted the interior structure of bone, have still reference to the forces acting on the bone" Most writers name the year 1886 as the start of the more scientific study of the structure of cancellous bone Professor Culmann, professor of engineering at Zürich, is said to have had occasion to enter the dissecting room of his anatomical colleague, Professor Meyer, and there happened to notice a longitudinal section of the head of a femur Culmann had just been designing a crane and at once recognised the arrangement of the bony trabeculæ as nothing more or less than a diagram of the lines of stress In fact he is said to have cried out "That is my crane" Culmann and an anatomist, Wolff, wrote a paper comparing the crane to the femur (Thompson 1942)

Actually, Culmann, Meyer, and Wolff were anticipated by nearly half a century by a little-known Englishman In 1838 F O Ward published in London a little book called *Outlines of Human Osteology* This work has not received the attention it deserves—at any rate not in Oxford, for when I took the copy out of the Bodleian Library the pages were uncut Ward pointed out that the neck of the femur resembled a wall bracket in which some members are in tension and some in compression He described this clearly in the text, and illustrated it with the drawing shown in fig 2

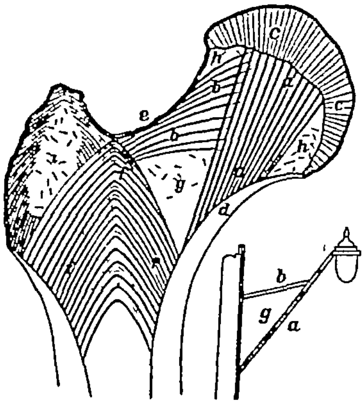

Fig 2—Drawing from Ward (1838) comparing the trajectories femoral head with a wall bracket. In both figures the mem are in compression and the members *b* in tension

When a block of any material is subjected to force, it temporarily changes its shape because of its elastic properties These small changes are called strains, and the internal forces which resist the deforming actions of the external forces are called stresses A strain is a linear movement, that is a matter of direction, but a stress is a force measured across an area of a plane Whatever the nature of the external forces—tension, pressure, or shearing—and however complicated, at every point in any plane section there are two directions of principal stress, always at right angles to one another The stress in one direction is the maximal tension, and the other the maximal pressure In the direction of the principal stresses there are no shearing stresses, but these will be present in any other direction It is thus [illegible] draw lines on any imaginary section of a body along the direction of probable stress These lines a be straight or curved, but at all points in the bod two sets of lines remain at right angles to each other, the closer they are together in any region, the greater probable stresses in that region, and vice versa fundamental idea in the trajectorial theory of b structure is that the trabeculæ of cancellous bone fo the line of trajectories in a homogeneous body of same form as the bone, and stressed in the same w This was the theory based on Culmann's crane an Meyer's section of the femoral head The theory however, been criticised on the ground that the tr tories are lines drawn from a number of arbit selected points at certain distances from each o If all possible lines were drawn, the diagram would completely black, for the number of possible traject is infinite In bone, therefore, we reach the parado conclusion that if trajectories and nothing else determ the arrangement of the trabeculæ all cancellous b would have to be compact bone Something els required to account for the existence of a lattice struc at all Another objection is that if trabeculæ do cross at right angles, they are not trajectorial A any bone section a number of trabeculæ can be se cross at angles other than 90° On the other hand, of the trajectory diagrams of bones consider only transmission by the bone (for example the femur) of body-weight and take no account of the numerous complicated stresses produced by muscular act Whatever the rights and wrongs of the traject theory, the trabecular arrangement of bone is modi by the stresses to which bone is subjected An elabor anatomical and mathematical analysis of the hu femur by Koch (1917) has shown beyond doubt stresses do determine the thickness, closeness of spac and arrangement of the trabeculæ

Apposition and Resorption

Bone is a form of connective tissue consistin ground substance and collagen fibres, in which have deposited crystals of a calcareous material which re the structure more rigid than the other tissues of body The collagen fibres of bone are continuous the rest of the connective tissues of the body, w indeed form continuous sheets of tissue, and is no reason to think, as far as microscopy or chemis can tell us, that bone collagen is substantially diffe from any other sort of collagen fibre This vie supported by the fact that bone can be laid down in varied tissues as the eye, meninges, tonsils, lu thyroid, ovaries, fallopian tubes, uterus, penis, kid arteries, operation scars, muscles, fascia, and tend It is only right to say that ectopic ossification oc only as the result of some pathological process and in the presence of the reactive proliferation of young connective tissue or granulation tissue It is not the type of pathological condition but the regenerative process common to all that counts

The bone cells or osteocytes have long protoplasmic processes which communicate with the adjacent Haversian canal and with the processes of other nearby bone cells The life of bone depends on its osteocytes If an osteocyte dies or is killed resorption takes place If the process is extensive resorption takes so long that a piece of dead bone separates—i.e the patient develops a sequestrum

The life of an osteocyte depends in turn on the availability of blood supply In the bone of dogs the maximum distance of an osteocyte from a capillary is 0 2 mm and most are within 0·1 mm That is why a large trabecula more than 0·2 mm across usually has a central blood vessel (Ham 1952) It also explains why bone, in common with other vascular tissues is very susceptible to interference with its blood supply

There have been various controversies about the origin, nature function, and mode of action of osteoblasts and osteoclasts. It is now generally agreed that whatever the detailed answers to these questions it can be taken that the presence of osteoblasts on a bone surface means that bone is being laid down and the presence of osteoclasts that it is being resorbed These facts enable the histologist to say what processes were going on at the moment that the bone was killed or fixed Moreover bone carries in its structure indelible records of its past history When growth ceases a chemical change takes place in the lamina at the surface that gives a different staining reaction—the so-called cement line If the line is straight, it is called a resting line and means that growth ceased there and was then resumed If bone resorption is in progress the erosion by osteoclasts is irregular, causing dents in the bone—Howship s lacunæ If the process is then changed to growth by apposition the wavy cement line so caused is known as a reversal line It is often possible to see where a new Haversian system has invaded old ones and sometimes three generations of Haversian systems can be identified

It is generally agreed that all changes in the shape of normal bones, whether macroscopic or microscopic occur by resorption and apposition at bone surfaces. And the term surface must here be used in the widest and most literal sense because it includes not only the outside of the bone, the inside of the medullary cavity (if it is a *long bone*) and the surface of every *trabecula*, but *also* the inside of every Haversian canal and Volkmann s canal The reactive surface of bone is an immense area.

As about 99% of the calcium in the body is situated in the bones, it is natural to suppose that it forms a reserve that can be called upon to provide calcium for other purposes Calcium ions are of course concerned in such vital functions as neuromuscular activity and clotting of the blood In pregnancy and lactation, too requirements are great In starvation the body conserves protein iron sodium and potassium but the excretion of calcium and phosphorus continues at the same level as in normal circumstances Nevertheless, the blood levels of calcium and phosphorus remain normal so there must be a drain from the skeleton There is reason to think that this occurs equally from all bone surfaces Therefore the effects are much more obvious in cancellous bone than in compact bone. If one imagines a single lamina to be removed from say the compact bone of the shaft of the femur which is $^{1}/_{4}$ in thick, there would be no appreciable difference but the removal of a lamina from each side of a thin trabecula would be a much greater proportional change

The Organic Matrix

As I have said bone is first and foremost a variety of connective tissue It is calcified and rendered hard as a secondary phenomenon The fact that after death the mineral part of bone persists long after the organic part has disappeared must not delude us into neglecting the importance of bone matrix It is indeed the most important part of bone because, although it is possible to have histological bone without calcification, it is not possible to have bone at all without a scaffold of matrix The organic part of bone comprises over half its weight and about two thirds of its volume It is composed of cells osteocytes osteoblasts and osteoclasts, the collagen fibres and the cement substance

In immature bone—that is, in the young animal or in rapidly formed bone such as callus around a fracture—the collagen fibres are laid down in an irregular feltwork, so-called fibrous bone In adult bone and callus which has had time to rearrange itself the fibres are organised in regular laminæ so called laminated bone The laminæ show a remarkable arrangement of collagen fibres where alternate layers are at right angles to one another with other layers between them placed obliquely (Lacroix 1951) This device anticipates by a few million years reinforced concrete plywood and laminated plastics and gives great physical strength both in compression and tension

The fibrous nature of bone can be easily demonstrated by pricking it with a round sharply pointed instrument such as an awl The point makes a round hole but when it is withdrawn leaves a linear split, or cleavage line which indicates the general direction of the collagen fibres in the outer circumferential lamellæ (for general reviews, see Armstrong 1944 Weinmann and Sicher 1947 Ham 1953)

Study of the more minute structure of bone takes us into a microscopic and submicroscopic world of bewildering complexity but I would like to remind you of some of the established facts that have bearings on bone function The ordinary light microscope has a maximum resolution of about 2000 Å (1 Å is a ten millionth of a millimetre) The electron microscope has a maximum resolution of about 20 Å—that is about one hundred times that of the light microscope The light microscope enables us to distinguish bundles of collagen fibres. Studies by polarised light and X ray diffraction reveal indirectly the orientation of collagen fibres and bone crystals The application of electron microscopy has enabled the actual bone crystals to be measured and photographed (Robinson 1952) The sequence of events in bone formation seems to be that the osteoblasts *produce the primitive matrix after which phosphatase* appears in the cell and later in the matrix itself As the matrix matures collagen fibres appear and the cement substance undergoes changes that cause it to stain metachromatically Then but not before bone crystals are deposited and bone results The electron microscope also enables us to see clearly the differences in arrangement of the collagen fibres in fibrous and laminated bone

The Mineral Constituents

The mineral constituents of bone are equally complex (Huggins 1937 Nicolaysen Eeg Larsen and Malm 1953) The main constituent of bone mineral is a double salt of calcium phosphate and calcium carbonate (Logan 1940) For some reason that I have never been able to understand writers on this subject seem determined to show that this substance is the same as some known mineral dug up from the earth It has been variously identified with dahlite apatite hydroxyapatite and francolite. There is no biological reason why it should be a terrestrial mineral and equally no reason why it should not be a substance peculiar to bone

The skeleton contains not only 99% of the total calcium in the body but also 90% of the body citrate

80% of the body carbonate, 25% of the body sodium, and 8% of the body water. The citrate, carbonate, and sodium are thought to lie in the cement substance in relation to the surface of the calcium phosphate crystals. There can be little doubt that these constituents of bone other than calcium and phosphorus fulfil important physiological functions, but little or nothing is known of the details.

Bone crystals are blocks of about 500 × 250 × 100 Å lying in the cement substance and in alignment with the collagen fibres. The rigidity of bone is thought to be due to the adhesion of the crystals one to another, to adjacent collagen fibres, and to the protein molecules of the ground substance by the attraction of hydrogen bonds. Bone can undergo small plastic deformations in which the crystals slide over one another. The efficiency of this process depends on the physical state of the cement substance; hence the greenstick fracture of the child and the brittle bones of the aged. The ageing of bone matrix is similar to that of intercellular substance in other parts of the body—namely, a slow process of dehydration. The water content of young bone is 30% and of old bone only 20%.

Some idea of the size of bone crystals may be gained from the fact that if they were magnified until they were just visible to the naked eye, or 0·5 mm. across, a man's femur on the same scale would be about three miles along. Their small size gives them a large surface area. One gramme of crystals has a surface area of 106 sq. metres; so the total area of a man's bone crystals is nearly 100 acres. It might be supposed that this large area would make bone crystals chemically reactive; but, owing to their block-like shape and internal structure, only the outer layers, amounting to 12 to 14% of the whole crystal, are readily available for exchange. Neuman and Weikel (1954) have shown from measurement of the rate of molecular exchange of phosphate ions in different circumstances that it can be postulated that the most rapid rate occurs in the hydration shell that surrounds the crystal, a slower rate with the exchange from the hydration shell to the crystal itself, and the slowest rate of all to the exchange of surface ions with sub-surface ions. This explains the rapid immediate exchange of bone crystals with injected radiophosphorus and also the rapidity with which the radiophosphorus can leave the skeleton again. The main mass of bone crystal is not in fact very reactive. The sodium in the bone behaves in a similar manner. Only about one quarter is available for exchange with radiosodium, and equilibrium is reached with this moiety in about twelve hours. The unexchangeable portion is presumably bound to the crystals of bone mineral and is out of osmotic equilibrium with the body fluids (Miller and Wilson 1953, Edelman, James, Baden, and Moore 1954).

Metabolism

Information about the metabolic activities and the rate of turnover in bone has been obtained from experiments in animals with radioactive phosphorus (Hevesy 1940). Injected labelled phosphate disappears rapidly from the blood, and in two hours only 2% remains. Most of it goes into the extracellular fluid, but some to exchange with various organs. The loss by excretion is negligible in short experiments. Most of the phosphorus retained finds its way into the bones, and after three months 92% of the radioactive phosphorus remaining in the body is in the skeleton. This sounds a large amount, but only a small proportion of the bone phosphorus has exchanged with the radiophosphorus, because there is so much more phosphorus in bone than in blood—about a thousand times as much per gramme weight. As might be expected, the phosphorus uptake is greater in growing bone and in the epiphysis than in the diaphysis. Hevesy, Levi, and Rebbe (1940) administered radiophosphorus in frequent small doses so as to keep it radioactive inorganic-plasma phosphorus constant. Comparison of the radioactivity of bone with plasma, weight for weight, gives an indication of the renewal rate bone. By this method they found that after fifty 29% of the femoral and tibial epiphyses were renewed, but only 7% of the diaphyses. On the other hand, there was a 50% changeover in the scapula.

Since this work, other experiments, for example those by Jowsey, Owen, and Vaughan (1953) with radioactive strontium, have helped to explain these figures. Radio-strontium is taken up by the skeleton, as is calcium, and it is possible to make effective autoradiographs of bones by this means. These observations have shown the very patchy nature of bone building. Intense activity may be present in quite small areas, scattered about sometimes in an understandable manner, and sometimes for no apparent reason; but it is probable that we merely do not know the reason. This patchy activity of normal bone in space is paralleled by its variable activity in time. Bigwood (1952) has pointed out that a normal man may be in negative calcium balance for a few days, and then in positive calcium balance for a few days for no apparent reason, but no doubt depending on the algebraic sum of bone resorption and bone apposition. Experiments by Govaerts and Dallemagne (1948) with radioactive phosphorus have shown that, when medullary new bone is built, nearly half the phosphorus does not come from the freely available radiophosphorus fed or injected, but from phosphorus already stored in the skeleton. This reminds us of the constant turnover of phosphorus and calcium from bone surfaces for use at other sites. Conversely, experiments by Greenberg (1939) have shown that although phosphorus exchange occurs in the more vascular parts of bone, in the growing animal at any rate, it is not long before it is redistributed all over the skeleton. He estimated that the average stay of a phosphorus atom in the human body was thirty days.

It is important to realise, as Leblond, Wilkinson, Bélanger, and Robichon (1950) in Ottawa have pointed out, that there are two types of reaction of injected radiophosphorus with the skeleton. In the first, which they call "exchange," there is a rapid uptake and rapid release of phosphate. In the second, which they call "precipitation," there is actual formation of new bone, and the radiophosphorus persists at the site. These differences may well be due to exchange with the outer layers of bone crystal in the first instance and deposition of new bone mineral in the second.

Making Old Bones

The remoulding of the trabeculæ of the child to adult form is part of a process that continues every hour until the person's death. It is true that it takes place irregularly in space, but in every one of us there is at any given moment in some part of the skeleton active destruction going on, and elsewhere equally active rebuilding, with the expected result that from one year's end to another we show no substantial change. Nevertheless, over a period of years changes do occur because the skeleton, like other tissues, undergoes development and growth, enjoys an all too brief prime of life, and then suffers defervescence.

This brings me to the general question of how long a man should live from the biological point of view. In a state of Nature, the hazards of insufficient food, the depredations of enemies, and the perils of epidemic disease give many species a hard struggle to maintain their existence. Few animals survive long beyond the end of the reproductive epoch, even in the protection afforded by captivity. Indeed, some species have special mechanisms to bring about the death of the individual after reproductive powers have ceased.

The human species broadly speaking reproduction ceases in women about 50, and potency and fertility are greatly diminished in men after this age It might be argued that owing to the helplessness of human babies and children *they need parental protection* in the biological sense at any rate until nubile, that is to say about 15 years On these terms, Nature would not require us to survive much beyond the age of 65 and if we do so it is at our peril. But the prospect of life of a baby born today is about 59 years for a boy and 63 for a girl, and if *a man survive till 50 he has an average* chance of living to over 70, and a woman of 50 till nearly 75

It might be supposed that Nature would provide mankind with a body that operated with reasonable efficiency till the end of the reproductive epoch because after that the individual is of no consequence as regards continuing the species Common observation shows that there is something in this view The degenerative diseases—cardiac ischæmia cerebral ischæmia cataract osteo-arthritis and the like—are uncommon before 50 and become increasingly prevalent thereafter You will recollect that Osler spoke of the comparative uselessness of men over 40 and the complete uselessness of men over 60. It is after 50 that mankind turns to spectacles false teeth, hearing aids and the other modern devices for making the latter half of life physically tolerable It is not surprising that the skeleton shares in this depressing involution.

Various attempts to assess the normal age changes in the skeleton have been made. It happens that Western Reserve University and Washington University St Louis, possess between them over 4000 carefully documented skeletons collected respectively by Dr Todd and Dr Terry By documented is meant that the age sex race, occupation, and medical history of the former owner of each skeleton is known This is a unique collection of material and has been carefully studied by Ingalls (1931) and others. Briefly total skeletal weight rises from 25 to 30 years falls at 45 rises to another peak at 55, and then steadily declines to 70 and no doubt beyond "The peak at 35 is regarded as the prime of physical life and the decline that follows marks the beginning of deterioration of bony tissue the first real age change a gradual lightening of the bones an increase in their porosity and accentuation of some of the fine surface markings. In a word the bone is past its prime and those physical *characters which enable it to perform its* function and determine its specific gravity and weight suffer a gradual recession from the previous high water mark" (Ingalls 1931)

The second rise to 55 is probably spurious and accounted for by new bone formation around the articular surfaces and in the skull and axial skeleton The final fall carries the total skeletal weight to its lowest adult point The bone becomes light and porous loses some of its elasticity and its factor of safety diminishes

It is this osteoporosis that I wish in particular to describe and discuss.

Osteoporosis Defined and Distinguished

The first of the many difficulties that we encounter is that of terminology Many writers follow Humpty Dumpty—"When *I* use a word it means just what I choose it to mean"—and the literature of metabolic bone disease abounds in loose and apparently little understood terminology

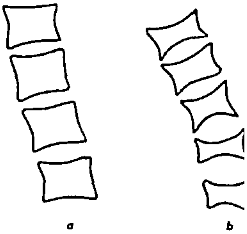

Fig 3—Drawings from X-ray films the outlines of (a) normal and (
osteoporotic centra.

The general term *decalcification* is used to describe X ray appearances or post *mortem findings* in which the bones appear to be deficient in mineral salts, or are unduly thin soft or brittle and there is no *clear reason for this* occurrence These changes may be due either to too little bone substance or to made quately calcified bone matrix Decalcification is not in itself an undesirable term but it is usuall possible to be more precise

Osteomalacia—literally softening of the bones—is use to describe the condition of the bones arising fro deficiency of calcium or vitamin D or both The clinic picture X ray changes, biochemical findings histologic features and treatment are wholly specific for th condition and it is plainly undesirable to use the ter for any other disease Nevertheless, the word is ofte used as a synonym for osteoporosis in such phrases senile osteomalacia and even postmenopausal oste malacia There are of course no such diseases and th patient either has osteomalacia from deficient calcif cation of osteoid tissue or he has not

Osteoporosis—literally porosity of bone—is likewis used loosely to mean decalcification of unknown ætiolog but since the work of Albright (1947b) has come to hav a specific meaning The term is now reserved for the deficiency of bone arising from insufficient matrix formation in the presence of normal calcification of osteoid tissue As the term has a clearly defined meaning it is most desirable that its use should be kept precise and reserved for the condition of inadequate bone formation from lack of matrix.

Halisteresis—literally deprivation of salt—is a term that has been used to describe the state (now believed to be non-existent) where bone mineral is removed leaving osteoid tissue or uncalcified matrix There is no evidence that such a state of affairs ever occurs and if bone is destroyed the destruction involves matrix and mineral equally and *simultaneously* The *only objection to this* general rule is the observation of Ham (1952) that in a Howship s lacuna it is sometimes possible to see in the concavity a minute brush like fringe which could be interpreted as the ends of collagen fibres projecting from

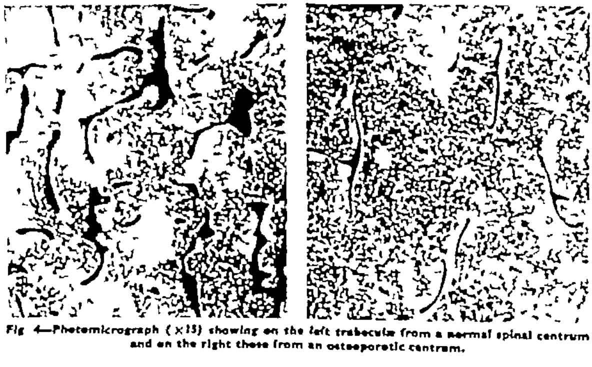

Fig 4—Photomicrograph (×15) showing on the *left* trabeculæ from a normal spinal centrum and on the right those from an osteoporotic centrum.

the bone under destruction There is certainly no evidence of any widespread demineralisation of matrix as a feature of natural bone resorption or pathological bone destruction The term halisteresis has therefore died out in English and American writings, though it has lingered on in France and South America Like the other terms, it is liable to misuse

The distinction to which I particularly wish to draw your attention is that between *osteoporosis* and *osteomalacia*, because here confusion of terminology may lead to confusion of diagnosis, and hence to the wrong treatment of patients

Strictly speaking, osteoporosis is a pathological diagnosis and can be made with certainty only by the morbid histologist, but there are a number of clinical features and X-ray appearances which often justify this diagnosis in the living

The salient feature of the morbid anatomy is that there is atrophy of bone The trabeculæ are fewer and thinner than normal In the spine this causes the centra to shrink and be compressed, chiefly in their central part, so that they become biconcave (so called "fish vertebræ") The intervertebral discs expand and become biconvex (fig 3) The nucleus can absorb water and enormously increase in size, exerting great pressure as it does so These expanded discs and Schmorl's nodes can occur together The spine as a whole shows a rounded kyphosis and is shorter than normal The osteoporotic deformities, which are slight in the neck, become increasingly evident from above downwards and are usually most advanced in the lumbar region

The histological picture is that there is simply too little bone what there is consists of bone of normal structure (fig 4) It may be in the state of undergoing resorption, of being stationary, or of growing by apposition of new matrix and new bone

(To be concluded)

A MORPHOLOGICAL CRITIQUE OF TEMPORAL LOBECTOMY

L Crome

M C, B Com Edin., M.R C.P E

NEUROPATHOLOGIST, THE FOUNTAIN HOSPITAL, LONDON

The diagnosis of "temporal lobe" epilepsy is being made more frequently and the practice of temporal lobectomy is growing As the case in favour of this operation rests partly on the discovery of lesions in all the resected lobes (Earle et al 1953, Falconer 1954, Meyer et al 1954, Liddell and Northfield 1954), it may be useful to record findings which throw doubt on the significance of these structural abnormalities

The abnormalities recorded are of two kinds (*a*) lesions with distinctive features (such as tumours, cysts, hamartomata, and scars) usually circumscribed and obvious to the naked eye, and (*b*) lesions with less easily defined morphology, usually diffuse and only apparent microscopically The latter form the majority—14 in the series of 18 of Meyer et al (1954) and 100 in the 157 of Earle et al (1953) They consist mainly of meningeal fibrosis, cellular proliferation in the white matter, sclerosis of the Ammon's horn, cortical atrophy, and subpial gliosis, one variant of which is the "incisural sclerosis" mentioned by Earle and his colleagues

This paper presents evidence that similar lesions can be found occasionally in the temporal lobes of people with no epilepsy, that when they occur in epileptics they are not confined to one of the temporal lobes, and that they are quite common in mental defectives whether or not these have fits

Temporal Lobes in Non-epileptics

The temporal lobes of 29 non epileptic patients (controls) were examined for microscopical diffuse lesions. Coronal blocks were embedded in celloidin, and sections 20 µ thick were prepared and stained with cresyl violet and with phosphotungstic acid and hæmatoxylin

It became obvious at once that, if the lesions were only slight, their detection was a very subjective matter Judging by the illustrations provided in the biopsy reports cited above, many areas of the temporal lobes of several of these controls were likewise pathological, while some showed greater abnormality (tables I and II) Further, neither of the above-mentioned stains gave consistent results always It therefore proved necessary to record some results as doubtful

Table I shows that in 8 non-epileptic patients the following structural abnormalities were found in the temporal lobes meningeal fibrosis (6), subpial gliosis (6), cortical atrophy, including diffuse cellular degeneration (5), and gliosis of white matter (4) No sclerosis of the Ammon's horn was observed

Table II shows that in 21 non epileptic but mentally defective patients the abnormalities were fibrosis (13), subpial gliosis (15), cortical atrophy (15 gliosis of white matter (16), and sclerosis of the Ammon' horn (5)

The lesions were more conspicuous in the brains of the mental defectives, but except for sclerosis of Ammon's horn, they were also present in the brains of the mentally normal patients

Temporal Lobes in Epileptic Mental Defectives

I have previously described (Crome 1954) the findings in the brains of 61 mentally defective [illegible] with epilepsy Their mental condition made cl[illegible] of fits uncertain, but the fits were described as major 40, minor in 5, mixed in 5, atypical in 2, and unspecif in 9 Psychomotor phenomena, hallucinations, and nature of any aura could not, of course, be ascertained Electro encephalography was done in 7 cases All records were abnormal but none were described characteristic for "temporal lobe" epilepsy all cases there was some structural abno (table III)

For the present purposes this material was re[illegible] to decide whether the temporal lobes had been affected in any special way Sections of the celloidin embedded material were available in 30 cases (table IV)

As expected, every temporal lobe presented some abnormality, and usually many Comparison of these, however, with lesions elsewhere in the brain made obvious that, apart from sclerosis of the Ammon's horn in 9 cases, none was peculiar to the temporal lobe, nor was there evidence of any significant difference in the extent and distribution of the lesions Moreover, all the lesions were bilateral, except in 2 cases with embolism of a middle cerebral artery, and in none were the lesions restricted to the temporal lobes

The only real difference between the structural abnormalities in the temporal lobes and in other areas was sclerosis of the Ammon's horn in 9 of these cases This is also one of the lesions found in biopsy specimens in "temporal lobe" epilepsy—e g, in 5 of the 14 cases reported by Meyer et al (1954)

Can this sclerosis mean that the fits originate in the temporal lobes? It seems unlikely, since it is well known that this lesion is often found in all forms of epilepsy and is nowadays generally considered to be the result and not the cause of fits—produced, perhaps, by anoxic episodes In the present series, as in many previously published cases, this sclerosis was associated with lesions, particularly sclerosis, in other areas of the brain, there appears to be no reason for attaching special epileptogenic importance to the Ammon's horn and the temporal lobes. Moreover, this sclerosis is by no means constant in biopsy specimens in "temporal lobe" epilepsy and it occurs occasionally in the absence of epilepsy (see above)

TABLE III—THE MAIN STRUCTURAL ABNORMALITIES IN THE BRAINS OF 61 EPILEPTICS

Abnormality	No of cases	Abnormality	No of cases
Reduction in weight	53	Absence of corpus callosum	[illegible]
Ventricular dilatation	46	Atrophic changes associated with retrolental fibroplasia	2
Localised agenesis or atrophy	31	Pachygyria	2
Ulegyria	22	Fusion of frontal lobes	2
Cysts and cavities	18	Mongolism with cerebral abscess	2
Changes of uncomplicated mongolism	1	Mongolism with embolism	[illegible]
Localised or diffuse induration	18	Marked cerebellar sclerosis	2
Fibrosis of meninges (macroscopical)	7	Lipidosis	1
Microgyria	6	Changes associated with gargoylism	1
Tuberous sclerosis	5	Porencephaly	1
Calcification	3	Megalencephaly	1
Obstructive hydrocephalus	2	No gross abnormality	0
Arhinencephaly	2		

It remains to consider what relation these abnormalities in the brains of epileptics who are mentally defective bear to epilepsy in persons of normal intelligence. Though this must be largely speculative, in my experience such lesions, although often more severe, are not usually different in kind from those in other chronic cerebral disorders. Mental defectives with extremely deranged brains present lesions which often are only much magnified reproductions of conditions in more normal people. Hence it would be reasonable to expect in this series lesions characteristic of "temporal lobe" epilepsy. The absence of any significant localisation in the temporal lobe suggests that lesions in biopsy material are also probably not confined to one temporal region. This was so in the single example coming to necropsy in the series of Meyer et al. (1954): changes in one temporal lobe were seen after resection, but similar changes were discovered in the opposite temporal lobe after death.

Structural changes described in biopsy material by previous workers fell, as mentioned above, into two groups—discrete and diffuse. My material suggests that

TABLE IV—STRUCTURAL ABNORMALITIES IN THE TEMPORAL LOBES OF 30 EPILEPTICS

Abnormality	No of cases	Abnormality	No of cases
Reduction in size	24	Microgyria	4
Subpial gliosis	22	Fibrosis of meninges	[illegible]
Partial or localised agenesis or atrophy	15	Tuberous sclerosis	3
Cortical cellular atrophy	21	Calcification	3
Increase in number of glial cells in white matter	20	Pachygyria	2
Ulegyria	12	Softening due to embolism	2
Cysts and cavities	10	Lipidosis	1
Sclerosis of the Ammon's horn	0	Changes associated with gargoylism	1

TABLE I—STRUCTURAL FEATURES IN TEMPORAL LOBES OF NON-EPILEPTIC PATIENTS OF NORMAL INTELLIGENCE

Case no.	Sex	Age (yr.)	Clinical features	Meningeal fibrosis	Subpial gliosis	Cortical atrophy	Gliosis of white matter	Sclerosis of Ammon's horn	Chief additional features
1	M	38	Acute poliomyelitis	+	+	−	Doubtful	−	Staining unsatisfactory
2	M	57	Meningovascular syphilis	+	+	+	±	−	Staining unsatisfactory
3	M	42	Lymphosarcoma of meninges	+	+	+	Doubtful	−	Nissl staining unsatisfactory
4	M	39	Acute poliomyelitis	Doubtful	+	−	±	−	
5	F	30	Subarachnoid hæmorrhage	+	+	+	−	−	
6	M	33	Acute perivenous encephalitis	−	+	+	+	−	Lesions of perivenous encephalitis not present in temporal lobe
7	F	44	General paralysis of insane treated with malaria	+	Doubtful	++	+	−	Staining unsatisfactory
8	M	17	Acute poliomyelitis	+	−	−	−	−	

TABLE II—STRUCTURAL FEATURES IN TEMPORAL LOBES OF NON-EPILEPTIC MENTALLY DEFECTIVE PATIENTS

Case no.	Sex	Age (yr.)	Clinical features	Meningeal fibrosis	Subpial gliosis	Cortical atrophy	Gliosis of white matter	Sclerosis of Ammon's horn	Chief additional features
9	M	25	Congenital mental defect feeble-mindedness diabetes	+	++	±	−	±	
10	M	1	Unclassified congenital idiocy	−	+	+	+	+	Generalised cortical atrophy
11	M	14	Mongolism imbecility	+	+	±	+	−	
12	M	2	Microcephalic idiocy terminal meningitis	+	+	+	+	−	
13	F	3	Slight microcephaly patent foramen ovale idiocy	+	+	+	+	−	Marked disorientation of nerve cells
14	M	7	Moderate microcephalic idiocy	−	±	±	−	−	
15	M	11	Gargoylism	+	+++	++	+++	−	Distension and ballooning of nerve-cells meningeal cellular infiltration
16	M	60	Unclassified feeble-mindedness	Doubtful	Doubtful	+	Doubtful	−	Staining unsatisfactory
17	F	2	Microcephalic imbecility	++	++	Doubtful	+	−	Increase of capillaries in white matter Nissl staining unsatisfactory
18	M	7	Idiocy possibly caused by Rh incompatibility	+	++	±	+	−	
19	M	7	Obstructive hydrocephalus	++	+++	++	++	±	Ventricular granulations
20	F	21	Microcephalic imbecility with diplegia	+	++	+	+	+	Marked neuronophagia
21	M	[illegible]	Mongolian imbecility	Doubtful	Doubtful	+	Doubtful	−	Staining unsatisfactory
22	M	[illegible]	Idiocy possibly caused by Rh incompatibility		++	++	+	+	Status marmoratus of thalamus
23	M	4	Slight microcephaly athetosis imbecility	−	Doubtful	+	+	−	
24	M	1½	Microcephalic idiocy		+	+	+	Doubtful	Pachygyria and microgyria
25	F	4	Mongolian imbecility	Doubtful	+	+	+	−	Status spongiosus of white matter
26	F	6	Hydrocephalic idiocy	+	±		+	−	
27	M	5	Unclassified imbecility		++	+	+	−	
28	F	5	Imbecility following tuberculous meningitis	++	+	++	+	+	
29	M	4	Mongolian feeble-mindedness	−	Doubtful	+	Doubtful	−	

Indefinite results due to unsuccessful staining are marked as doubtful, results doubtful in spite of satisfactory staining as ±, and positive ones +, ++ and +++ in order of severity.

lesions may be expected elsewhere in the brain when either type is detected in a single temporal lobe, since, except for tumours, they were all represented here and were always widely scattered

Discussion

This study throws doubt on the significance of certain lesions found on biopsy and alleged to account for most cases of "temporal lobe" epilepsy Such diffuse and microscopic abnormalities occur in the temporal lobes of patients with no such clinical picture, moreover, their detection is unreliable

The study also indicates that, in mental defectives with epilepsy, brain lesions are neither peculiar nor confined to the temporal lobes The material further suggests that, in "temporal lobe" epilepsy, lesions when present in one temporal lobe will be accompanied by others elsewhere in the brain in many cases

The material in this report is small, and further observations are clearly necessary to determine what constitutes normal variation, and what these structural abnormalities signify It is possible, however, to reach some preliminary conclusions

It has long been known that certain cases of focal epilepsy are associated with lesions, usually circumscribed, such as tumours and scars, in one of the temporal lobes The current extension of this concept to a large number of other cases seems to lack sufficient morphological evidence It is still particularly necessary in any given case to exclude lesions outside the affected temporal lobe, even where an abnormality in the latter is beyond question In most cases the clinical relevance of whatever deviations are seen under the microscope has yet to be established The present study suggests that their importance may be slight

I appreciate, of course, that the modern concept of "temporal lobe" epilepsy rests not on morbid anatomy alone but also largely on the reported value of temporal lobectomy But the findings recorded here indicate the need for careful reconsideration of the basis of clinical assumptions

Summary

The increase in temporal lobectomy is based partly on the examination of resected tissue, abnormalities being recorded in every published case, but the significance of such abnormalities is doubtful

The microscopical appearances forming the sole abnormality in most of the published cases are not peculiar to "temporal lobe" epilepsy They depend on subjective assessment and inconsistent methods of staining, and, where slight, are not always pathological

Whenever indisputable abnormality exists in one temporal lobe it is likely to be associated with lesions elsewhere in the brain and, possibly, in the opposite temporal lobe Usually, therefore, disease will not be eradicated by removal of a single temporal lobe

The presence of certain lesions in the temporal lobes does not prove their responsibility for epilepsy or other symptoms

Further observation to determine what constitutes normal histological variation is necessary before importance is attached to certain microscopical findings

I am greatly indebted to my lay and medical colleagues at the Fountain Hospital for their help, access to case records, and discussion of this report

REFERENCES

Crome L (1954) *Proc R Soc Med* 47, 850
Earle K M Baldwin M, Penfield W (1953) *Arch Neurol Psychiat Chicago* 69 27
Falconer M A (1954) *Brit med J* ii 939
Liddell, D W Northfield D W C (1954) *J Neurol Psychiat*
alconer M A Beck F (1954) *Ibid* p 276

EFFECT OF ADRENALINE ON ADRENOCORTICAL SECRETION

J D Hunter*
M B N Z, M R C P
MEDICAL REGISTRAR, POSTGRADUATE MEDICAL SCHOOL, LONDON

R I S Bayliss
M D Camb, M R C P
ASSISTANT PHYSICIAN WESTMINSTER HOSPITAL, LONDON

A W Steinbeck
M.D Sydney, M R C.P, Ph.D Lond
LECTURER IN MEDICINE, UNIVERSITY OF QUEENSLAND

From the Department of Medicine, Postgraduate Medical School of London

When the adrenal glands are healthy, the administration of corticotrophin is usually followed by a fall in the eosinophil-count in the peripheral blood (Thorn et al 1948, Forsham et al 1948) Since this eosinopenia does not develop in addisonian patients but can be produced by giving both normal and adrenalectomised people pure adrenocortical hormones, there is good evidence that it is related to increased adrenocortical activity This relationship has been confirmed by the simultaneous changes in the eosinophil-count and in the level of adrenocortical hormones in the blood after the administration of corticotrophin (Nelson et al 1952, Gemzell and Franksson 1953, Hunter et al 1955)

The injection of adrenaline may also cause eosinopenia in man and laboratory animals This response likewise has been attributed to increased adrenocortical activity because it is not observed to the same degree either in untreated addisonian patients or in adrenalectomised mice (Laragh and Almy 1948, Recant et al 1950, Speirs and Meyer 1949, Bisso 1953) Recant et al (1950) observed a mean change of –62% (range from –40% to –80%) in the eosinophil count of healthy people after an injection of 0 3 mg of adrenaline, whereas in 11 patients with untreated Addison's disease the mean change was only –21% (range from +20% to –44%)

Increased amounts of adrenocortical hormones have been reported in the venous blood of the adrenal glands of dogs and cats after the infusion of adrenaline, and in rats adrenaline depletes the ascorbic acid and cholesterol of the adrenal glands (a response taken to indicate increased adrenocortical secretion) (Vogt 1944, Long and Fry 1945, Pickford and Vogt 1951)

These changes do not take place in hypophysectomised animals, hence it has been suggested that adrenaline enhances adrenocortical activity indirectly by stimulating the hypothalamus and thence the pituitary gland to secrete increased amounts of corticotrophin These observations form the basis for the adrenaline test of pituitary-adrenal function proposed by Recant et al (1950)

The validity of this concept has been called in question since the observation by Muehrcke et al (1952) that, whereas in untreated addisonian patients the injection of adrenaline does not cause significant eosinopenia, it produced a significant fall in the eosinophil-count of 36–78% in 5 adrenalectomised patients receiving constant cortisone maintenance therapy, although the administration of corticotrophin induced no change in the eosinophil-count This suggested that the presence of adrenocortical hormones was necessary for adrenaline to cause a significant eosinopenia, but that the eosinopenia was not directly due to increased adrenocortical activity

The study reported here was undertaken to find out whether the eosinopenia following the administration of adrenaline was due to increased adrenocortical secretion judged by direct measurement of the plasma level of adrenocortical steroids and by comparing the response

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* New Zealand travelling medical scholar

TABLE I—PLASMA LEVELS OF 17 HYDROXYCORTICOSTEROIDS AND EOSINOPHIL-COUNTS AFTER INJECTION OF ADRENALINE

Case no.	Sex	Age (yr)	Adrenaline (mg)	Minutes after injection														Eosinophil-count					
				0	1	2	3	4	5	6	7	8	9	10	15	30	60	Initial count (per c.mm.)	Percentage change (hr after injection)				
				Plasma level of 17 hydroxycorticosteroids (µg per 100 ml)															1	2	3	4	6
1	M	27	0·3	17							14				13	9		141	−44	−61	− 0	−48	−48
2	M	46	0·3	3					8					4	6	18	13	337	+6	−22	−28	−13	−17
3	F	17	0·3	9							16				24	11		437	+13	−59	−79	−81	−59
4	F	25	0·3	14							17				19	16		160	0	−64	−64	−64	−36
5	M	28	0·3	9	12		12		10					16				469	−13	−57	−48	−38	−21
6	M	38	0·4	8	8		6	9				7			11			537		−60		−67	42
7	M	31	0·5	6		8		7		17			7		13			156		−76		−68	−40
8	M	56	0·3	7					7					6	6	5		131	+9	−33	−28	0	+43
9	M	27	0·3	27					22						25	31		204	[illegible]	−55	−51	−60	−24
10	M	37	0·3	6					9						7	9		575	+9	−34	−34	−30	
11	M	26	0·3	5		6			9					9	9			125	−5	−35	−50	−35	−20
12	M	21	0·3	10	9		8		12		8			7				375	−5	−28	−42	−33	−17
13	M	65	0·3	6		7		5		8		7		8	8			187	+10	−17		−1	+44
14	M	31	0·3	11		13			13		11			13	14			73	−16	−41	−51	−51	−41
15	M	28	0·5	17			13							16	14	16		402		−61		−60	−23
16	M	34	0·5	7			4								11	9		181		−64		−79	−72
																		Mean	0	−48	−50	−47	−25

to adrenaline with those to single intravenous injections of corticotrophin

Material and Methods

Corticotrophin 30 units dissolved in 10 ml of saline solution was injected intravenously over 5 minutes into 5 people, and adrenaline 0·3–0·5 mg subcutaneously into 16 people of whom most were healthy colleagues but a few were convalescent patients These observations were controlled by eosinophil-counts after an injection of saline solution in 12 people in many of whom eosinophil-counts had previously been made after the injection of adrenaline

All the observations were made between 10 A.M and 4 P.M The eosinophils in peripheral blood obtained from a finger and stained by Randolph's method, were counted hourly for 6 hours by one observer (J D H) For each count two leucocyte counting pipettes were used, and two Fuchs Rosenthal counting-chambers were filled from each.

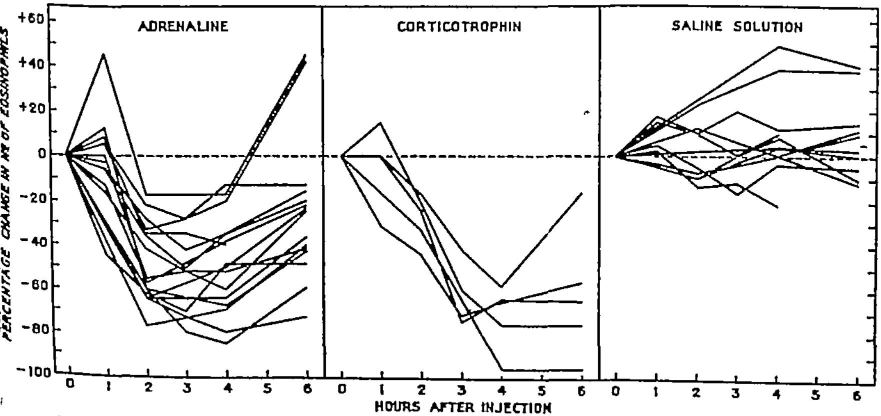
The plasma level of 17 hydroxycorticosteroids was measured by the method of Nelson and Samuels (1952) modified by Bayliss and Steinbeck (1953) The accuracy of this method is such that a rise or a fall of 4 µg per 100 ml of plasma can be considered a significant change.

Results

Adrenaline

The results are shown in table I and the accompanying figure In most of the people adrenaline produced pallor, tremor and palpitations In all of them the eosinophil count fell to a minimum at 2–4 hours after the injection but to widely different amounts ranging from −17% to −84% (mean −55%) The mean falls 2 3 and 4 hours after the injection of adrenaline were 48%, 50%, and 47% respectively

The plasma levels of 17 hydroxycorticosteroids, which are known to cause eosinopenia were determined in multiple samples of blood taken during the first 30 minutes after the injection Particular attention was paid to this time because the observations of Kelley et al (1952) Sandberg et al (1953) and Ly et al (1954) published while our investigation was in progress had not shown any increase in plasma-steroid levels 1–4 hours after the injection of adrenaline, and because previous studies had shown that after an intramuscular injection of corticotrophin the peak of the plasma-steroid level was about 2 hours before the greatest fall in the eosinophil-count (Nelson et al 1952, Gemzell and



Percentage changes in numbers of eosinophils after injection of (1) adrenaline (2) corticotrophin, and (3) saline solution

TABLE II—PLASMA LEVELS OF 17-HYDROXYCORTICOSTEROIDS AND EOSINOPHIL-COUNTS AFTER A SINGLE INTRAVENOUS INJECTION OF 30 UNITS OF CORTICOTROPHIN

Case no	Sex	Age (yr)	Hr after injection							Eosinophil-count					
			0	1/4	1/2	1	2	3	4	Initial count (per c mm)	Percentage change (hr after injection)				
			Plasma level of 17 hydroxycorticosteroids (µg per 100 ml)								1	2	3	4	6
17	F	30	18	15		28	28			112		−33		−95	[illegible]
18	M	36	10	18	20	22	37	24	11	50	0	−24	−74	−64	[illegible]
19	M	52	13	16	38	23	30	23	20	144	−31	−44	−72	−65	[illegible]
20	M	58	6	17	13	25	30	26	19	106	0	−17	−41	−59	[illegible]
21	M	45								125	+15	−20	−60	−75	[illegible]
										Mean	−4	−28	−62	−71	−6

Franksson 1953, Hunter et al 1955) Hence it was argued that if the eosinopenia, which is severest about 2 hours after the injection of adrenaline, were due to increased adrenocortical activity the plasma steroid level would be expected to rise within the first few minutes after the injection

No consistent change in the plasma level of 17 hydroxycorticosteroids was observed In case 1 the eosinophil-count fell by 70% and the plasma-steroid level from 17 µg to 9 µg per 100 ml In 6 people (cases 2–7) the plasma steroid level rose by more than 4 µg per 100 ml, and in each instance there was eosinopenia, the greatest change in the eosinophil-count ranging from −28% to −84% (mean −63%) In contrast 9 people (cases 8–16) showed a change in the eosinophil-count ranging from −17% to −79% (mean −48%) without any change in the plasma-steroid level beyond 4 µg per 100 ml

For example, case 14, whose eosinophil count fell by 51%, had strikingly little variation in the plasma steroid levels The mean maximal fall in the eosinophil-count was not statistically greater in the people whose plasma-steroid level rose than in those in whom it did not change ($t=1\ 245$)

Control Observations

No consistent changes in the eosinophil count were observed in the 12 controls over the 6 hours' observation, and in none did the eosinophil count fall by more than 22% (see figure)

Intravenous Corticotrophin

The results are shown in table II and in the figure The greatest fall in the eosinophil count took place 3–4 hours after the injection, and the mean falls at 2, 3, and 4 hours were 28%, 62%, and 71% respectively The plasma steroid level rose significantly 1 hour after the corticotrophin had been given, and in some people it rose within 15–30 minutes

Discussion

These results show that the fall in the eosinophil count induced by adrenaline is unrelated to increased adrenocortical activity, because the degree of eosinopenia was the same whether or not the plasma steroid level rose Furthermore the *greatest fall in the eosinophil count* did not take place until 3–4 hours after a single intravenous injection of corticotrophin, whereas *it took place at least an hour earlier after an injection of adrenaline* If adrenaline caused eosinopenia by releasing corticotrophin, one would expect the eosinopenia after the injection of corticotrophin to reach its maximum as soon as or sooner than, after the injection of adrenaline The injection of adrenaline was not followed by a detectable rise in the plasma level of 17 hydroxycorticosteroids in 10 of 16 people The rise in the plasma steroid level in 5 was much less than that usually observed after the injection of corticotrophin Whether the increased adrenocortical activity observed in these 5 people was directly related to adrenaline or to some other factor, such as emotion, must remain undecided, but in view of the findings of Sandberg et al (1953) it is clear that in man adrenaline does not necessarily cause increased secretion of adrenocortical hormones

On the available evidence it seems that the presence, rather than an increase, of adrenocortical hormones is necessary for adrenaline to lower the eosinophil count more than 50% (Muehrcke et al 1952, Henry et al 1953) But, even *in the presence of normal plasma*-steroid levels, 5 of our subjects did not show an eosinopenia *of this degree, and Fisher and Fisher* (1951) have also emphasised that healthy people often have no significant eosinopenia after the administration of adrenaline Therefore, if a person's eosinophil-count is lowered more than 50% by the administration of adrenaline, *adrenocortical* function is probably normal If, on the other hand, it is not lowered so much, no conclusions can be drawn Furthermore in other circumstances—e g, after severe burns and after trauma—the eosinophil count cannot be used as a valid index of adrenocortical function

Summary

Adrenaline causes a variable degree of eosinopenia which is maximal 2–4 hours after the injection, whereas after the intravenous injection of corticotrophin the eosinopenia is maximal after a delay of 4 hours

The eosinopenia after the injection of adrenaline is unrelated to any rise in the plasma level of 17 hydroxycorticosteroids

These observations suggest that, in man, adrenaline does not cause increased adrenocortical secretion

REFERENCES

Bayliss R I S, Steinbeck A W (1953) *Biochem J* **54**, 523
Bisso, A (1953) *J clin Endocrin* **13**, 1226
Ely, R S, Bray P F, Rallo, R B Kelley, V C (1954) *J clin Invest* **33**, 1587
Fisher, B Fisher E R (1951) *Amer J med Sci* **221** 121
Forsham P H Thorn G W Prunty F T G, Hills, A G (194
J clin Endocrin **8** 15
Gemzell C A, Franksson C (1953) *Acta endocr, Copenhagen*, 14 205
Henry W L jun, Oliner, L, Ramey, E R (1953) *Amer J Physiol* **174** 456
Hunter J D Bayliss, R I S, Steinbeck, A W (1955) In *preparation*.
Kelley V C Ely, R S Rallo R B, Bray, P F (1952) *Proc Soc exp Biol, N Y* **81**, 611
Laragh J H, Almy T P (1948) *Ibid* **69**, 490
Long C N H, Fry, E G (1945) *Ibid*, **59** 67
Muehrcke R C, Staple T W, Kark R M (1952) *J Lab clin Med* **40** 169
Nelson D H Samuels L T (1952) *J clin Endocrin* **12**, 519
— Sandberg A A, Palmer, J G, Tyler, F H (1952) *J clin Invest* **31** 843
Pickford, M Vogt, M (1951) *J Physiol* **112** 133
Recant, L Hume D M, Forsham, P H, Thorn, G W (19
J clin Endocrin **10** 187
Sandberg A A Nelson D H Palmer, J G, Samuel, L T Tyler, F H (1953) *Ibid*, **13** 629
Speirs, R S Meyer R K (1949) *Endocrinology* **45** 403
Thorn, G W Forsham, P H Prunty, F T G, Hills A G (19
J Amer med Ass **137**, 1005
Vogt M (1944) *J Physiol* **103**, 317

CORTISONE, CORTICOTROPHIN, AND INFECTION

A. G. SHAPER
M.B. Cape Town, D.T.M. & H.

A. DYSON
M.B. Lpool

MEDICAL REGISTRARS, CLATTERBRIDGE HOSPITAL, BEBINGTON, CHESHIRE

THE tendency for cortisone and corticotrophin to enhance bacterial infections has been noted as one of the most important complications of therapy with these hormones.

Coste et al. (1951) estimated that 10% of patients so treated developed infective complications, especially staphylococcal abscesses at the site of injection and acute pneumonia. Dubois-Ferrière (1951) described a case of staphylococcal septicæmia in a patient under treatment with cortisone, and Page (1954) reports two cases of fulminating pneumonia in patients treated with corticotrophin and with cortisone.

In the following two cases fatal staphylococcal septicæmia supervened.

Case reports

Case 1.—A woman was diagnosed as having acute rheumatoid arthritis in 1946 at the age of 30. While on treatment with Myocrisin she developed at the site of injection a staphylococcal abscess which required incision. In June, 1954, she was admitted for two months with an exacerbation of her arthritis and a mild erythematous rash over the forehead and malar regions. She had intermittent pyrexia and showed no clinical response to treatment with mepacrine and chloroquine. Her intermittent pyrexia persisted until October, 1954, when she was readmitted with active arthritis and much loss of weight. On the basis of her skin lesions and the course of her illness, as well as laboratory investigations, disseminated lupus erythematosus was diagnosed. From the time of her readmission in October, 1954, the intermittent pyrexia continued and on Nov. 4 her temperature was 101·4°F. Examination revealed rhonchi and occasional râles over both lung fields, and treatment with crystalline penicillin 500 000 units six-hourly was started and continued until Nov. 7.

Cortisone Therapy.—On Nov. 5 concomitant therapy with cortisone 200 mg. daily was begun. Her general condition improved rapidly, and her temperature became normal for the first time in three weeks and remained so for the following eight days. On the ninth day of cortisone treatment (Nov. 13) she spent the morning walking about the ward. At 2.30 P.M. her temperature was found to be 103·8°F and at 6 P.M. it was 102·2°F. She vomited a little on one occasion but otherwise felt well. Examination revealed no physical signs of disease. At 10 P.M. her temperature was 103°F and pulse-rate 150. At 6 A.M. next morning she was found comatose with temperature 103°F and blood-pressure 100/50 mm. Hg and unresponsive to stimuli. She had no signs of meningeal irritation, and all her limbs were equally flaccid, with normal plantar responses. She was given crystalline penicillin 1 000 000 units immediately and 500 000 units six-hourly thereafter. By 10 A.M. her respirations had become stertorous, her blood-pressure had fallen to 70/40 mm. Hg, and there was slight neck rigidity. Lumbar puncture revealed a turbid fluid under normal pressure and containing 1200 cells per c.mm., mainly polymorphs, total protein 120 mg. per 100 ml., and sugar 50 mg. per 100 ml., and a stained film showed polymorphs but no organisms. There was no growth after twenty-four hours' culture. The patient was given intrathecal penicillin 10 000 units. Her blood-pressure continued to fall, and an infusion with noradrenaline in 5% glucose-saline solution was started, which produced a temporary rise of blood-pressure, but her condition deteriorated and she died at 10.45 P.M.

Necropsy Findings.—The brain showed no gross changes beyond slight congestion of the meninges. The liver was considerably enlarged (72 oz.) and showed fatty change. The spleen was enlarged (13 oz.) and very soft. Both kidneys were of normal size; on their cortical surfaces were numerous small petechial hæmorrhages and multiple small abscesses. Abscesses were also found in the substance of the kidney, from which a penicillin-sensitive *Staphylococcus aureus* was grown. Death was due to staphylococcal septicæmia.

Case 2.—A man aged 50 was admitted in September, 1953, with primary exfoliative dermatitis. Cortisone therapy was instituted, and he was maintained on an average dose of 100 mg. daily. In March, 1954, corticotrophin therapy was started in addition to the cortisone, an average of 75 mg. of corticotrophin and 50 mg. of cortisone being given daily. This dosage was varied from time to time, and by November, 1954, the patient was receiving 50 mg. of corticotrophin and 50 mg. of cortisone daily, and his skin was improving. From his admission until November, 1954, his condition remained fairly satisfactory, and he was ambulant and complained only of cutaneous irritation. In March, 1954, he had developed a typical moon facies, which persisted. On Nov. 19 he developed over his right elbow a superficial abscess which discharged spontaneously and healed. A small inflammatory nodule on the dorsum of his left hand also cleared spontaneously. On the evening of Nov. 26, while at rest in bed, he developed severe precordial pain which radiated down both arms and was associated with considerable dyspnœa. The lung fields were normal on examination, heart sounds were faint, and heart size could not be estimated clinically. Myocardial infarction was diagnosed and was confirmed by electrocardiography. In view of the skin condition treatment with cortisone and corticotrophin was continued. Two days later the patient became more dyspnœic and slightly confused. He was found to have auricular fibrillation and received digitalis, which had little effect on the heart-rate. The dyspnœa persisted for several days, but there was no further chest pain, and the patient was conscious and able to eat his meals. On Dec. 3 his condition deteriorated rapidly, and in three or four hours he became semiconscious. Towards evening his temperature rose to 102°F, and he was given crystalline penicillin 500 000 units six-hourly; he developed Cheyne-Stokes respiration and died next day.

Necropsy Findings.—Meningitis was present, with a collection of thick yellow pus covering the undersurface of the brain. The pericardium was grossly distended by thin yellow pus, and the left ventricle was considerably hypertrophied. In the interventricular septum were much scarring and fibrosis associated with hæmorrhage into the septum. Two small abscesses were found in the myocardium. Both kidneys were of normal size and contained several small abscesses in their substance. *Staph. aureus* was grown from the pus in the pericardial cavity and from the myocardial abscesses. Death was due to staphylococcal septicæmia.

Discussion

Experiments on animals have given the impression that uncontrolled infections following treatment with either cortisone or corticotrophin are a result of overdosage; that this is not necessarily so is shown by one of the cases described by Page (1954) which had been treated with 20 mg. of corticotrophin gel for seven days, and by the present case 1, in which 200 mg. of cortisone was given daily for nine days.

The causes of infections in patients treated with either corticotrophin or cortisone are not clear; but whatever the primary cause, the result is a disturbance of the host-parasite relationship in favour of the parasite.

The practical problems are those of prophylaxis, early diagnosis, and suitable treatment. The routine administration of a broad-spectrum antibiotic as a prophylactic does not recommend itself to most physicians, and regular weekly diagnostic blood-cultures will only give a false sense of security. Regular clinical examinations are most important in the search for symptomless infections, and any clinical signs of disease should be fully investigated by radiography, blood-counts, and blood-cultures.

There is both experimental and clinical evidence that in patients under treatment with either corticotrophin or cortisone antibiotics may become relatively ineffective. The reason for the need for larger doses of antibiotics than usual may, however, be a consequence of late diagnosis due to the masking of symptoms and not of some intrinsic effect of cortisone on antibiotics.

Consideration should be given to the use of somatotrophic hormone (growth factor) in the prevention the treatment of infections in patients under treatment with either corticotrophin or cortisone Selye (1951) considered on theoretical grounds that this factor might act as an antagonist to the infection-spreading action of corticotrophin and cortisone, and his experiments on animals have shown that this action can be completely prevented by suitable doses of purified somatotrophic hormone Lewis (1953) reports that this work has been confirmed by H J Robinson The somatotrophic hormone and preparations containing several principles of the anterior lobe of the pituitary gland in combination with somatotrophic hormone are available commercially, and it should be possible for centres treating large numbers of patients with corticotrophin and cortisone to make a controlled investigation into this possibility

Summary

Two cases of staphylococcal septicæmia complicating treatment with corticotrophin and cortisone are described

The use of somatotrophic hormone in prophylaxis and treatment of such infections is suggested

We wish to thank Dr F J Zacharias and Dr D G Freshwater, under whose care these cases were admitted, Dr M. W W Wood and Dr Zacharias for their encouragement and advice in the preparation of this paper, and Dr H MacLean for the necropsy reports

REFERENCES

Coste F, Piguet B, Galmiche, P, Cayla, J (1951) *Ann Méd Paris* 52 747
Dubois-Férrière H (1951) *Pr méd* 59, 442
Lewis, T (1953) *Ann N Y Acad Sci* 56 799
Page, J A (1954) *Brit med J* ii, 1334
Selye H (1951) *Canad med Ass J* 64, 489

A SINGLE-STAGE METHOD OF FREEZE-DRYING ARTERIES FOR GRAFTING

T H FLEWETT
M D Belf
LECTURER IN BACTERIOLOGY IN THE UNIVERSITY OF LEEDS

K. S ZINNEMANN
M D Frankfurt
SENIOR LECTURER IN BACTERIOLOGY IN THE UNIVERSITY OF LEEDS

M W C OLDFIELD
M.B E, M A, D.M, M Ch Oxfd, F R C S
SURGEON, GENERAL INFIRMARY, LEEDS, AND ST JAMES'S HOSPITAL, LEEDS

H. S SHUCKSMITH
B Sc, M B Leeds, F R C S
ASSISTANT SURGEON, UNIVERSITY OF LEEDS

F DEXTER
TECHNICIAN, GENERAL INFIRMARY, LEEDS

WHEN we found that arterial grafts deteriorated when kept for three or four weeks in the solution of Gross et al (1949), we carefully studied the method of freeze drying described by Eastcott et al (1954) of St Mary's Hospital London, because it originated from the first active artery bank to be established in this country

Our previous experience over the past eleven years with freeze-drying of bacterial cultures has enabled us to simplify the technique of the St Mary's Hospital team further to a single stage operation

Apparatus

and Rubber Stopper with s (Tube Head)—The tube

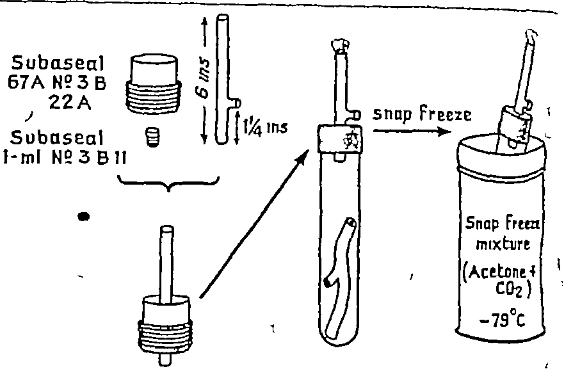


Fig 1—Drying tube and apparatus for snap-freezing

for the artery is of 'Pyrex' glass 25 cm long with an inside diameter of 32 ± 1 mm It is sterilised, plugged with cotton wool, and, when autoclaved, is ready for the surgeon to collect the arteries The construction of a rubber stopper carrying a suitable smaller pyrex glass tube to allow evacuation of the large pyrex tube, permanent sealing after completion of the freeze drying, and a simple sterile method of reconstituting the dried artery is shown in fig 1 The rubber stopper used is a 3 B 22A type 'Subaseal' artery graft closure turnover 67A with a central perforation, the broader uppermost flange of this bung rides on the rim of the large pyrex tube thus preventing the bung from being sucked inside by the high vacuum present at the end of the freeze drying A side-arm is blown on to a length of narrow pyrex glass tubing (15 cm long with an outside diameter of 9 mm) about 3 cm from one end of this smaller tube, and the diameter of the short side arm is standardised to give an airtight fit with a small rubber bung, which is either a standard subaseal 3.B.11 type turnover (1 ml) vial closure or a subaseal turnover *closure 13H B.H drab The short end of the 15 cm* narrow pyrex tube—now a T tube—is inserted into the central perforation of the large rubber stopper, and the opposite end of the tube is closed either with a cotton wool plug or a standard subaseal 3 B 16 utility cover cap 9 All these parts assembled form the "head" of the tube containing the graft, tube and head together form the "drying tube." The complete head is wrapped up in lint and sterilised by autoclaving at 15 lb pressure for 30 minutes The flange of the sterile head should be moistened with a few drops sterile liquid paraffin to ease insertion into the mouth of the pyrex tube containing the artery

Vacuum Equipment—The essential parts of the equipm —vacuum pump, moisture trap, and manifold for the dr tubes—are shown in fig 2 The pyrex glass manifold connected in series by pressure tubing with a moisture tr and a single stage rotary vacuum pump (Edwards 1 S.15 protected by a phosphorus pentoxide trap The manif has an outside diameter of 18 mm and seven side arms 30 mm long, each having an outside diameter of 15 mm To six the side arms a pyrex glass high vacuum stopcock with 10 mm. bore is connected by rubber pressure tubing, and these are attached the drying tubes The seventh side-arm is permanently connected to a Pirani gauge head The high vacuum stopcocks enable each drying tube to be individu connected to the apparatus and sealed off from it with accidentally breaking the vacuum of the whole system.

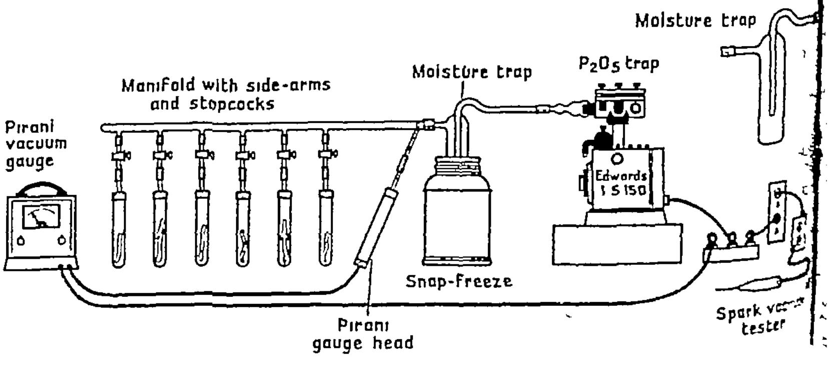


Fig 2—Vacuum equipment for freeze-drying

Method

Collection of Arteries—People aged less than 30 who have died from either trauma or poisoning are selected within six hours of death Extensive patchy atheroma may be found even at this age, and only arteries which are regular in their consistence to palpation when empty are used for freeze-drying if patches of atheroma are felt, the arteries are stored in Gross's solution An aseptic technique is used to remove the whole aorta and the external iliac and femoral arteries as far as the origin of the popliteal arteries by an extraperitoneal and transpleural approach The abdominal aorta is divided at the level of the renal arteries and the external iliac arteries are divided at the origin of the femoral arteries the resulting four pieces of tissue are put in four sterile pyrex tubes whose ends are closed with sterile cotton wool. The tubes are taken to the department of bacteriology at once and freeze-drying started, or else they are stored overnight in a refrigerator whose temperature is maintained at +4°C

Sterilisation.—As an additional precaution the arteries are sterilised on arrival at the laboratory by treatment with a 1% solution (v/v) of liquid ethylene oxide (B D H) Since ethylene oxide boils at 10·7 C and is explosive and rather toxic it must be stored in a refrigerator and handled in a cold storage room at +4 C with chilled syringes and needles. Each artery is covered with a measured quantity of sterile physiological saline solution at +4 C and for the sterile cotton wool plug is substituted a well fitting sterile rubber stopper Sufficient ethylene oxide is next added to give a 1% solution and the tube is inverted several times over the rubber stopper to ensure uniform solution of the ethylene oxide The tube is left at +4°C for one to two hours the rubber stopper is replaced by a sterile cotton wool plug, and the tube is placed in a fume cupboard at room temperature overnight to allow the ethylene oxide to vaporate The saline solution is next poured off under aseptic recautions the cotton wool plug is replaced in the mouth of ho tube and the whole is inverted in a refrigerator at +4 C o allow all residual moisture to drain into the cotton wool lug Small segments of the artery are next cut off under eptic conditions for aerobic and anaerobic sterility tests.

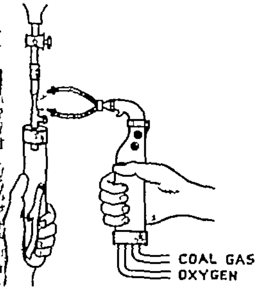


Fig. 3—Sealing of drying-tube in vacuo.

Snap-freezing—The tube containing the artery is fitted with ho bung with attachments and immersed in a mixture of olid carbon dioxide and acetone in a quart-size Thermos ar for 15 minutes (fig 1) The artery is then ready for mmediate drying or it can be kept in solid carbon dioxide t −79°C until it is convenient to dry it

Freeze-drying—Each stopcock is kept closed with the acuum pump running until the drying tube is connected o it the stopcock is next opened to obtain a high vacuum a rapidly as possible; sublimation of ice with consequent all of temperature prevents softening of the frozen artery he Pirani gauge shows the vacuum obtained and the amount f residual moisture at any given stage of the drying because o long as sublimation from the artery takes place water apour in the system will prevent the pressure from reaching ts minimum. When the limit of the vacuum pump under hese conditions is reached (about 0·01 mm Hg in the case of dwards Speedivac 1S 150) it is assumed that no more ublimation will take place and that drying is complete but o be on the safe side the vacuum pump is allowed to run for nother one to two hours, during which the Pirani gauge hould remain steady

Sealing in Vacuo—Immediately before the sealing of each rying tube its vacuum stopcock is closed to prevent accidental ontamination of the other tubes still attached to the manifold. The 15-cm glass tube of the head is next sealed above its side arm with a Chance's Flame Master cross fire burner using coal gas and oxygen (fig 3) and cautiously tested for high vacuum with a spark tester Care should be taken that the spark does not cause a leak in the glass The sealed head of the tube is next protected by a Viskap seal which comes well down the neck of the tube and a viskap sleeve with printed instructions for reconstitution of the grafting material is finally put round the body of the tube

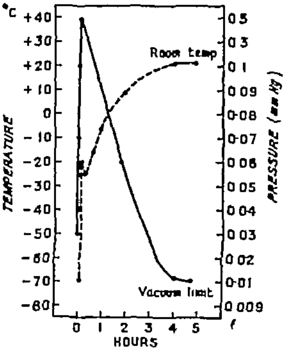


Fig 4—Relationship between temperature and vapour pressure within evacuating system during freeze-drying of a piece of femoral artery measuring 0·5 × 15·0 cm.

Reconstitution—The viskap seal is removed and the exposed surface of the subaseal turnover closure (1 ml vial) occluding the short side-arm is sterilised with either iodine or antiseptic triple dye A sterile blood transfusion giving set is attached by sterile rubber tubing to an infusion bottle containing saline solution with penicillin 100 units per ml and streptomycin 100 μg per ml If desired, heparin (2 ml per 100 ml) may be added to the reconstituting fluid The needle is next pushed through the side-arm closure Owing to the high vacuum the drying tube fills easily with the solution. Reconstitution is complete within twenty minutes.

Efficiency of Method

Technical—For a rough assessment of the temperature changes taking place during drying an alcohol thermometer was fitted in an airtight manner into one of the subaseal artery graft bungs the tip of the thermometer was manœuvred into the lumen of the frozen artery; and the temperature was read at regular intervals These readings, and those of the Pirani gauge which we used as an indication of the progress of drying were plotted against time Figs 4 and 5 show graphs obtained in this way during the drying of a piece of femoral artery measuring 0·5 × 15·0 cm and of a piece of abdominal aorta measuring 2·0 × 15·0 cm The graph obtained by processing a main arterial tree—e.g thoracic aorta abdominal aorta with both iliac arteries and the two femoral arteries—differs very little from that obtained with the 15-cm piece of aorta. The curves, as may be expected are flatter when large pieces of tissue are dried It takes less than five hours to dry completely one femoral artery twelve to thirteen hours to dry a piece of aorta 15 cm

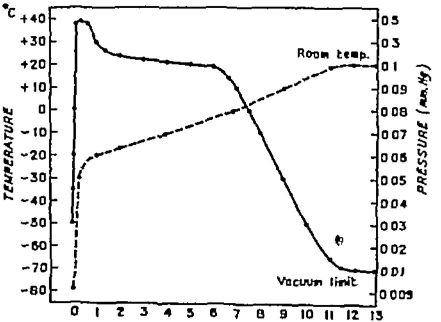


Fig 5—Same relationship as in fig 4 during freeze-drying of a piece of aorta measuring 2·0 × 15·0 cm.

long, and fourteen to fifteen hours to dry an arterial tree in one operation The actual temperature of the drying arteries is probably a little lower than the readings obtained, owing to the error introduced by external conduction of heat along the inserted thermometer, but absolutely accurate measurement of the temperature was thought to be less important than a general impression of the efficiency of the system, which is well demonstrated by the graphs The freezing mixture in the thermos container surrounding the moisture trap remains at –79°C for more than twenty-four hours, it is therefore possible to continue the drying overnight without any attention if it is not completed by the end of a working day

Bacteriological —Sterility tests are made aerobically in nutrient broth and anaerobically in Robertson's chopped meat broth, these media, inoculated with small segments of artery, are incubated for five days These and all other manipulations which require exposure of the artery are done inside an ultraviolet hood as used in virus and tissue culture work Thus contamination is excluded as much as possible So far only once has a femoral artery proved to be not sterile owing to having touched the outside of the large pyrex tube accidentally when samples were taken for sterility tests

Clinical —The reconstituted material is easy to handle, and the patient's clinical progress after the grafting of an aortic bifurcation prepared in this way is just as good as after that of a graft stored in Gross's solution

Discussion

The method of freeze-drying arterial grafts described by Eastcott et al (1954) does away with the necessity for keeping the grafts at low temperatures during most of the process, and with increasing the temperature subsequently to eliminate residual moisture, as has been necessary hitherto for satisfactory freeze drying of tissues' Their method, though simpler than those used by Marrangoni and Cecchini (1951) and Hufnagel (1954), consists of three stages (1) primary drying in vacuo of frozen arteries, (2) release of the vacuum, and secondary drying over phosphorus pentoxide, and (3) secondary evacuation and sealing in vacuo with 'Picien' high-vacuum wax after perforation of the rubber stopper with an aspiration needle

By the use of a special but simple closure head for the tubes in which the material is dried, of a pyrex-glass manifold with high-vacuum stopcocks between its side arms and the drying-tubes, and by the insertion of a deep cooled moisture-trap between the vacuum pump and the manifold, the process has been reduced to a single operation

Sterilisation with 1% ethylene oxide is not essential and can be omitted Though it has a moderate bleaching effect, ethylene oxide does not affect the elastic quality of the arterial wall We hope that ethylene oxide treatment will eventually permit us to dispense with strict aseptic precautions during collection, as advocated by Hufnagel (1954) This may ease the difficult task of finding suitable donor material, indeed Hufnagel states that ethylene oxide treatment renders heterologous arterial grafts acceptable to recipients

Eastcott et al (1954) state that fatty lesions in an atheromatous plaque invalidate the freeze-drying, so we use only grafts which are not atheromatous—i e, in which no thickenings can be felt, which is indeed a coarse method Atheromatous grafts can be kept indefinitely under deep freeze conditions at –79°C or stored for three or four weeks in Gross's solution with more safety The point is well illustrated by histological examinations made by Dr T W Sutherland on an aorta from a donor aged 39 A section cut before processing showed no abnormality a section cut after treatment with ethylene oxide showed very slight atheroma with a looser texture of the intima, and a section cut after reconstitution showed a still looser texture and prominent disrupted patches presumably due to overstretching of the intima over fatty deposits during drying It remains to be determined whether freeze dried grafts with slight atheromatous infiltrations might not be used successfully

The cost of the complete equipment, excluding rubber bungs and pyrex tubing, is about £130 One 25 cm pyrex tube costs 3*s* 9*d*, and one special rubber bung fitting into it about 5*s*., but both these parts can be used again many times, thus making a saving on the rubber bung compared with the method of Eastcott et al (1954) because they cannot use their perforated bung a second time

Summary

By the use of a special but simple closure head for the tubes in which the graft is dried, the insertion of a deep-cooled moisture trap between the vacuum pump and the manifold, and the provision of high vacuum stopcocks between the manifold and the drying tubes, arterial grafts may be freeze dried in a single operation in five to fifteen hours Once the freeze drying process has been started, the apparatus requires no further attention until sealing

The arteries are sterilised with a 1% solution of liquid ethylene oxide in saline solution Special precautions are required for handling this substance

We wish to thank Dr T W Sutherland and Dr W Goldie for providing us with post-mortem arteries for experimental purposes, Messrs Wm Freeman & Co (SubaSeal Works Barnsley) for making experimental types of rubber closures to our specifications and manufacturing the one finally chosen and Messrs Ralph Cuthbert (Huddersfield) for assisting us with the design of the pyrex glass parts of the earlier equipment We gratefully acknowledge a grant towards expenses given by the Board of Leeds United Hospitals One of us (K Z) is indebted to the Medical Research Council for a grant in aid of expenses

REFERENCES

Eastcott H H G, Holt L B, Peacock J H Rob, C G (19 *Lancet* i 1311
Gross R E Bill A H jun Peirce F C jun (1949) *Surg Gyn Obstet* 88 680
Hufnagel, C A (1954) Preservation and transplantation of nor tissues Ciba Foundation Symposium
Marrangoni A G Cecchini L P (1951) *Ann Surg* 134, 977

COMPRESSION OF THE ULNAR NERV AT THE WRIST BY A GANGLION

B L Mallett
M B Lond
FORMERLY NEUROLOGICAL REGISTRAR

K J Zilkha
M B Lond
FORMERLY NEUROLOGICAL HOUSE PHYSICIAN

GUY'S HOSPITAL, LONDON

TRAUMATIC neuritis of the ulnar nerve, giving rise t paralysis of the small muscles of the hand, has bee described for many years In most cases the site of th lesion is at the elbow More recently it has been recogni that the nerve may be damaged locally, at the wri or in the palm, and that then there is often a history occupational trauma

Anatomy

The ulnar nerve in the hand divides into a superfic division, which is often entirely sensory (or may cont motor fibres to the palmaris brevis muscle), and a de motor division, which at once disappears deeply betwe the abductor digiti minimi and the flexor digiti mini muscles It passes laterally behind the tendinous ori of the short flexor and perforates the opponens dig minimi muscle

Branches —The branch to the abductor muscle ar from the deep division just before the latter sinks into th hypothenar eminence The branch to the short flex muscle may arise at the same level, occasionally from common trunk Often it arises lower down, after th deep division has disappeared behind the short flex muscle Branches, occasionally two or three, to th opponens muscle arise as the deep division perforates th muscle (Hovelacque 1927)

Clinical Signs

Hunt (1908) described the clinical picture of involvement of the deep motor division with paralysis of all he small muscles supplied including the hypothenar roup The palmaris brevis muscle supplied by the uperficial division of the ulnar nerve was spared and here was no sensory loss

Seddon (1952) reported four cases of paralysis of the leep division of the ulnar nerve and cited twelve reviously published These differ from those described y Hunt (1908) in that in every case the hypothenar nuscles were spared Two patients gave a history of ulnar paræsthesiæ, one with pain but in no case was there any demonstrable sensory loss

Seddon notes that nearly all the patients were male half of them aged 40 or more the onset of the paralysis was either gradual or sudden and in almost all there was a clear history of trauma to the wrist or the palm, occasionally a single injury but more often repeated rauma connected with the patient s occupation Such ccupations included motor-cycling wire-cutting digging and the constant use of a leather knife held in the palm of the hand.

In one case, in an insurance agent with Dupuytren s contracture the palm was explored, but no constriction f fibrous tissue nor other compressing lesion was found

In five of the cases cited by Seddon an account of he subsequent progress is given (Russell and Whitty 947) These made a very good recovery in a few months cessation of the trauma held to be responsible

In the four cases observed by Seddon himself it was own for the first time that paralysis of the type escribed—i.e of all the small muscles supplied by the nar nerve excluding the hypothenar muscles and the almaris brevis muscle, and without sensory loss—may due to local remediable mechanical compression

In one of his cases there was tenderness medial to the ok of the hamate bone and in another crepitus on essure over the pisiform bone The latter also had pain d paræsthesiæ in the fourth and fifth digits

Seddon explored the wrists of all four In each he nd a small ganglion emerging from the palmar aspect a carpal joint and compressing the motor division the ulnar nerve distal to the branches supplying the othenar muscles. His patients made an excellent overy in 7–16 months.

Seddon suggests that the onset of paralysis either dual or sudden may be correlated in some cases h either gradual or sudden formation or enlargement a ganglion by herniation of the triquetral hamate novial sac Further such a ganglion may possibly ink spontaneously causing remission of the paralysis

Three cases of ganglionic compression of the ulnar rve with sensory loss as well as motor involvement re described by Brooks (1952) forming a distinct nical group

Two were in women aged 19 and 70 and one in a man aged The onset in each case was gradual, and in only one was re a history of trauma a fall on the outstretched hand e patient complained of ulnar paræsthesiæ and two had ellings, one tender in front of the wrist

All three had paralysis of all the ulnar intrinsic muscles e hypothenar muscles are not specially mentioned) and sory loss in the ulnar territory In each case a ganglion s found compressing the main trunk of the ulnar nerve ximal to its bifurcation into superficial and deep divisions.

There was good recovery in all three but a recurrence of the nglion after seven years demanded a further operation in case.

The original clinical picture described by Hunt 908), of involvement of all the ulnar intrinsic muscles the hand with no sensory loss has apparently not en been observed

We have recently seen two patients who presented in it such a way

Case reports

Case 1—A banker, aged 48 was admitted to Guy's Hospital under the care of Sir Charles Symonds. For twenty years he had written while standing at a high desk resting on the ulnar side of his wrist In the three months before admission he began to complain successively of pain in the right palm dropping his pen and then obvious wasting of his right hand

On examination (January 1954) there was moderate wasting of the interosseous muscles and slight wasting of the hypothenar muscles, with severe weakness of finger adduction and abduction including the abductor digiti minimi muscle and moderate weakness of the flexor digiti minimi brevis muscle There was no sensory loss. Pressure on the ulnar side of the pisiform bone caused local pain Radiography of the wrist showed evidence of osteo arthritis.

At operation Mr Grant Massie F.R.C.S found a ganglion compressing the main trunk of the ulnar nerve just proximal to its bifurcation into superficial and deep divisions. The ganglion was removed

Follow up—Five months later there was almost complete return of muscle bulk in the interossei and hypothenar muscles Power was virtually normal.

Case 2—A university lecturer aged 58 was admitted to Guy s Hospital under the care of Sir Charles Symonds. While acting in a play he had suddenly to extend his right wrist and to supinate his forearm fully flinging a person across the stage After the fifth performance he had pain in the hypothenar eminence Thenceforward he noticed gradually progressive weakness of adduction of the right little finger weakness of the fingers in holding a pen and weakness of grip

On examination (March 1954) two months after the onset there were wasting and severe weakness of the interosseous muscles and moderate weakness of the abductor digiti minimi muscle There was no sensory loss Radiography showed early osteo arthritic changes

At operation a ganglion as large as a small pea compressing the main trunk of the ulnar nerve was removed by Mr Massie

Follow up—Five months later the patient noted some improvement He could write better Healing of the wound had been delayed by trauma and infection but was now complete There was still obvious wasting of the interosseous muscles, with severe weakness of adduction and moderate weakness of abduction of the fingers, including the fifth

Discussion

A ganglion in front of the wrist joint may cause paralysis of the hand by compression of the ulnar nerve either its main trunk before bifurcation or its deep motor division Clinically it may present in one of three ways (1) paralysis of all the small muscles of the hand of ulnar innervation, with sensory loss in the ulnar territory (2) a similar paralysis with no sensory loss, and (3) with no sensory loss and with sparing of the hypothenar muscles

Our cases represent the second group Both men were aged more than 40 in both the onset was gradual and there was a history of trauma—in case 1 a chronic occupational trauma in case 2 repeated sudden unusual strain of the wrist joint—and in both radiography showed osteo arthritis

In neither case was there any sensory loss although at operation a ganglion was found compressing the main trunk of the ulnar nerve

After removal of the ganglion improvement was considerable in case 1 and slight in case 2

Summary

Three clinical types of paralysis of the hand due to ulnar nerve lesion at the wrist are discussed

All three may be due to ganglionic compression

When the ganglion is removed recovery from the paralysis is satisfactory

We wish to thank Sir Charles Symonds for his help and permission to publish

REFERENCES

Brooks D M (1952) *J Bone Jt Surg* 34B 391
Hovelacque A (1927) Anatomie des nerfs craniens et rachidiens et du système grand sympathique chez l'homme Paris
Hunt, J R (1908) *J nerv ment Dis* 35 673
Russell W R, Whitty C W M (1947) *Lancet*, i 828
Seddon, H J (1952) *J Bone Jt Surg* 34B 386

PAROXYSMAL MYOGLOBINURIA

MORRIS C BERENBAUM
L R C P E, D C P
REGISTRAR IN PATHOLOGY

C ALLAN BIRCH
M D Lpool, F R C P, D P H, D C H
PHYSICIAN

CHASE FARM HOSPITAL, ENFIELD, MIDDLESEX

J D MORELAND
B Sc Lond
POSTGRADUATE RESEARCH STUDENT, DEPARTMENT OF TECHNICAL OPTICS, IMPERIAL COLLEGE OF SCIENCE, LONDON

PUBLISHED cases of paroxysmal myoglobinuria have been reviewed by Acheson and McAlpine (1953), Elek and Anderson (1953), and Spaet et al (1954)

The last named collected 17 previously published cases, including 5 associated with muscular dystrophy, Gunther's (1924) case, which was almost certainly due to dermatomyositis, and the insufficiently documented case mentioned by Millikan (1939) They also include de Langen's (1946) case, omitting to mention that here myoglobinuria was due to exertion to the point of collapse, followed by a beating with a rifle butt in a Nazi concentration camp It was evidently a case of traumatic myoglobinuria

Hitherto 15 cases of myoglobinuria not associated with another muscle disorder have been published Many of the reports lack clinical details, making it uncertain that no other muscle disease was present, and in many there was no proof that the urinary pigment was myoglobin Of these patients 9 survived with little or no disability, sometimes after several attacks (Hittmair 1925, Debré et al 1934, Huber et al 1938, Hed 1947, 1953 [4 cases], Elek and Anderson 1953, Spaet et al 1954) The patient reported here also survives

The remaining 5 of the 15 patients whose cases have been previously published died *in an attack* (Paul 1924, Bywaters and Dible 1943, Schaar et al 1949, Buchanan and Steiner 1951, Stokes 1953) Death may take place within a few days, perhaps owing to the release of shock-producing substances from damaged muscle (Green 1943, Bielschowsky and Green 1943, Eggleton 1944, Green et al 1949, but see Kovách et al 1952) Other factors are involvement of respiratory muscles, pulmonary infection, and renal damage The cause of the renal damage is obscure it is probably a lower-nephron nephrosis (Bywaters and Dible 1943, Perri and Gorini 1952)

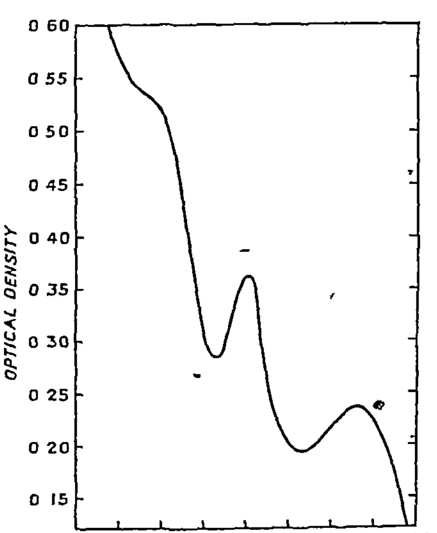


Fig 1—Optical-density curve of patient's urine cell depth 0 5 cm band width 4 mμ readings at 1 mμ intervals from 530 to 540 mμ from 575 mμ, and from 625 to 640 mμ elsewhere μ intervals.

Case-report

A girl, aged 10 years, complained of pains in both legs, and shortly afterwards abdominal pain and vomiting began There was abdominal and rectal tenderness Appendicectomy was done, and the appendix was found to be not inflamed On the day after the operation all the muscles becam painful and tender The urine was very dark brown an contained albumin, the guaiacum test was positive, but r red blood cells or porphyrin were present This fact, togeth with the history of muscle pains, suggested myoglobinur Examination with the Hartridge reversion spectrosco showed absorption bands judged to be at 583 and 635 m suggesting the presence of oxymyoglobin and a me compound

Progress —Four days after the onset the muscle pains ha gone, even though biopsy then showed gross changes Th patient recovered completely, and when last seen eight mon after the attack there had been no recurrence of sympto

Previous History —The patient was an adopted child an no family history was available At the age of 4 years sh had been admitted twice in one year to another hospital O the first occasion all that was found was "transient p teinuria" On the second occasion she had pains in the le and passed urine "like stout" She quickly recovered

Laboratory Investigations —Examination of the blo showed Hb 17 1 g per 100 ml, white cells 24,000 per c (polymorphs 92%), erythrocyte sedimentation rate 2 in 1st hr (Wintrobe), serum potassium (3 days after onset) 19 0 mg per 100 ml Lumbar puncture produced normal cerebrospinal fluid The serum-pseudocholinesterase level was within the normal range, hydrolysing 161 μ mols of acetylcholine bromide per ml per hr A glucose-tolerance test after the patient's recovery showed a normal curve with renal glycosuria Two days after the onset the 24 hr urinary output of creatine was 0 75 g creatinine 3 0 g, and of 17 ketosteroids 6 mg (normal 1 3-3 0 mg) The red cell fragility was moderately incre

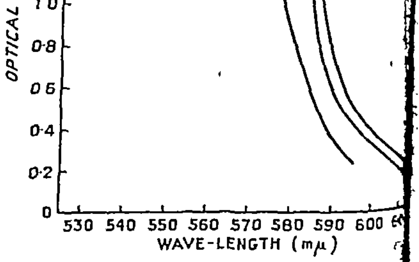


Fig 2—Optical-density curves of patient's urine myoglobin from human muscle (B) ; and globin (C), all converted to carboxy compo cell depth 1 cm ; band width 4 mμ, cur and B read at 1 mμ intervals from 535 to 5 and from 575 to 580 mμ curve C read at 1 intervals from 535 to 545 mμ and from 5 570 mμ readings elsewhere at 5 mμ interva

Percentage Saline Solution	*Percentage Hæmolys* *Patient*	*Healthy C*
0 55	0	0
0 52	6 5	1
0 50	18 0	2 5
0 48	39 0	9·0
0 44	86 0	51·0
0 42	96 6	76·0
0 40	100 0	86·0
0 30	100 0	100·0

Coombs's test, Ham's test for hæmolysis in acidified se Dacie's test for autohæmolysis on incubation, and Schumm for methæmalbumin were negative Reticulocytes were 1

Electrocardiography gave normal results, and el myography of several muscle groups twelve days after onset showed no abnormality

Spectroscopy of Urine —The patient's urine was exa in the Wright spectrophotometer Because of the spectrum in this instrument (20 cm between 400 and 700 and other features described elsewhere (Wright 1954) was no difficulty in taking readings at intervals of 1 Since the light absorption of normal urine increases fro red to the blue end of the spectrum, the beta band of ox globin shows in the present case only as an inflexion

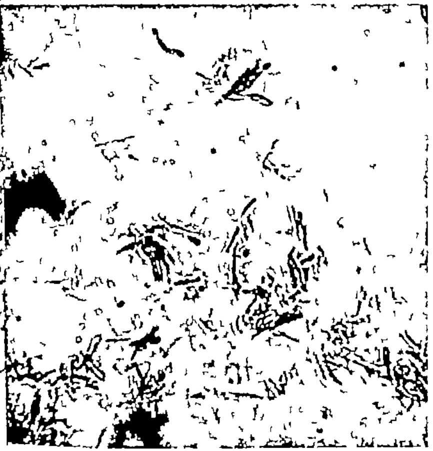


Fig 3—Crystals of metmyoglobin from patient's urine (×218)

urve at 540 mμ (fig 1) The alpha band of oxymyoglobin roduces a peak with a maximum at 580 mμ the peak at 0-632 mμ being that of metmyoglobin.

There are certain difficulties in the spectroscopic differentia on of oxymyoglobin and oxyhæmoglobin The alpha band axima are only 3–4 mμ apart and the beta band maxima -2 mμ apart Moreover exposure to air causes rapid oxidation metmyoglobin, with weakening of the alpha and beta nds and appearance of a non specific band at 630–633 mμ g 1) These difficulties are overcome by conversion of ymyoglobin and metmyoglobin to carboxymyoglobin. The pha-band maxima of carboxymyoglobin and carboxyhæmo obin are 10 mμ apart making their spectroscopic differentia on easy (fig 2)

Pigment	Position of Alpha-band Maximum Oxy Compound	 Carboxy Compound
moglobin	577 } 4 mμ apart	568 } 10 mμ apart
oglobin	581	578

Method (*after Blöck 1949*)—A spectroscope cell is almost led with the urine previously buffered to pH 8 and filtered al-gas is bubbled through it for 3–4 minutes a knife-point sodium hydrosulphite is added and the surface is covered ith liquid paraffin. Passage of coal gas is continued for other 3–4 minutes and the cell is covered with a lid The ition of the alpha band is then found with a reversion ectroscope, or the solution is compared with a solution of rboxyhæmoglobin in a comparison spectroscope Myoglobin s only a twenty fifth of the affinity of Hb for carbon onoxide and in contact with air is quickly converted to etmyoglobin If the cell is kept covered little change kes place for some hours

Estimation of Myoglobin.—We used Blörck's (1949) modifica n of de Duve's (1948) method to measure the myoglobin ntent of a biopsy specimen of one of the affected muscles her methods have been proposed by Shenk et al (1934) atson (1936) Beznák (1948) and Rossi Fanelli (1948) iefly the pigments are extracted from the muscle and nverted to carboxy compounds. Optical density is measured three wave-lengths, and the concentrations of myoglobin d Hb present are calculated from their respective extinction efficients Measurement of optical density after conversion pyridine hæmochromogen provides a check on the results e normal myoglobin content of human skeletal muscle is 3·0% of dry weight (Blörck 1949) In the present case ly 0·42% of myoglobin was present The results of measuring carboxy compounds and as pyridine hæmochromogen reed to within 4% The myoglobin content of the urine s about 1 mg per ml. or 1·5 g in the 24 hr output

Crystallisation—Methods for crystallising myoglobin from uscle are given by Theorell (1932) Bowen (1948) Rossi anelli (1949) Rees (1949) and Lawrie (1951) Theorell and de Duve (1947) crystallised myoglobin from urine in a case of myoglobinuria. We used the following methods, working at 0–4 C throughout:

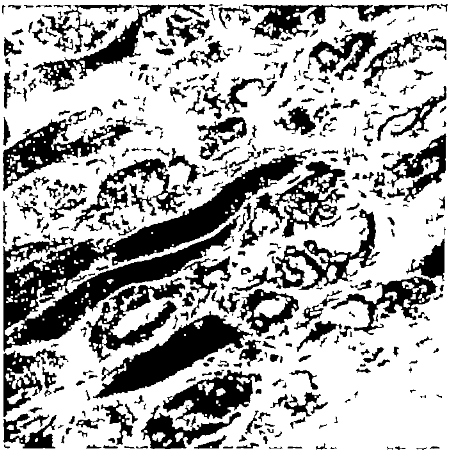


Fig 4—Muscle biopsy showing normal and degenerate fibres (Mallory's phosphotungstic acid hæmatoxylin ×186.)

(1) *After Rossi Fanelli (1949)*—Seitz filtered urine was dialysed against distilled water and then against numerous changes of 78% saturated ammonium sulphate at pH 6·8 It was next filtered and the brown filtrate was distributed in open petri dishes In a few days metmyoglobin crystals formed; most of them were spherical and very slightly birefringent with a tendency to split radially The spherical shape was probably due to impurities (R G Parrish personal communication) The rest were characteristically needle-shaped and birefringent sometimes several radiating from a common centre (fig 3)

(2) *After Rees (1949)*.—Seitz filtered urine was dialysed against distilled water next against 12% dextran to concentrate it, and finally against 3·5 *M* phosphate buffer of pH 6·4 The resulting dark brown syrupy liquid was left in an open test tube and gave again mostly spherical bodies together with a few cigar-shaped crystals

Histology—Four days after the onset of symptoms biopsy specimens of the left sacrospinalis muscle which was pale

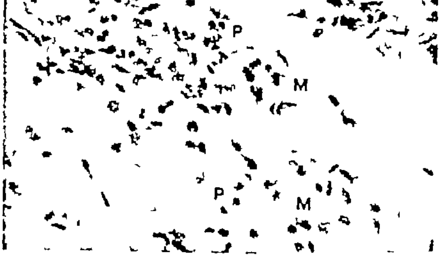


Fig 5—Muscle biopsy showing proliferation of sarcolemmal nuclei some of which are in mitosis (M); groups of polymorphs are present (P) (Hæmatoxylin and eosin. Glycol-wax embedding at 40 C. ×200)

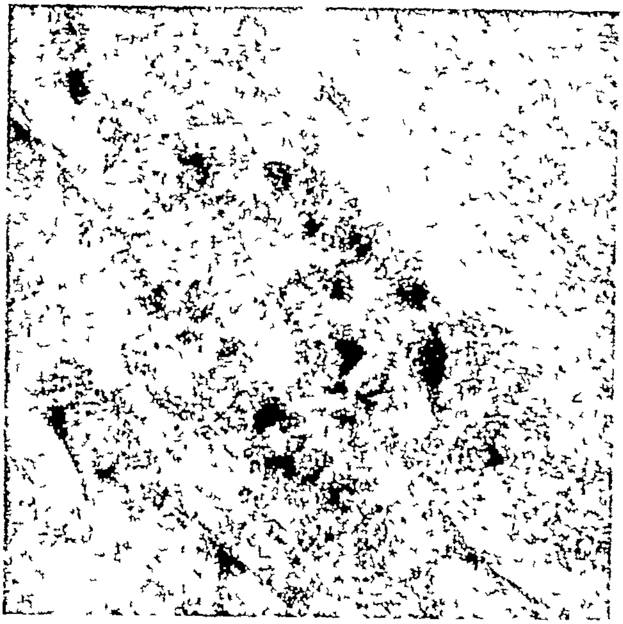


Fig 6—Muscle biopsy showing esterase in cytoplasm of sarcolemmal cells (Nachlas and Seligman's esterase method Formalin-fixed frozen section × 247)

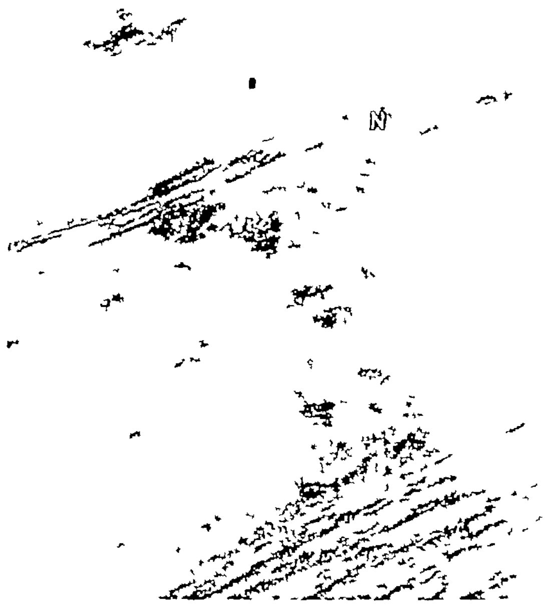


Fig 7—Muscle biopsy showing normal fibres (N), degenerate fibre intense granular birefringence (B), and optically inactive fi (Unstained paraffin section viewed between crossed polaroids. ×

soft, and swollen, and contracted poorly on stimulation, were fixed in formol saline solution, Helly's fluid, and alcohol, and paraffin-wax, glycol wax, and frozen sections were made Most of the tissue consisted of degenerate disrupted fibres with a few unaffected ones coursing among them The diseased fibres showed loss of striation, waxy degeneration, and fragmentation In a few places the muscle substance had contracted into a knot, leaving the sarcolemma empty and partly collapsed With Mallory's phosphotungstic acid hæmatoxylin, in contrast to the normal purple staining fibres, the degenerate fibres showed red brown complex coiled and branched figures in a pink matrix, while others showed pale blue homogeneous areas (fig 4) A few curled up strands still showed cross striation, more widely spaced than usual and without birefringence Stained with Masson's trichrome the degenerate areas were bright red, the empty sarcolemma blue and the normal fibres purple Abrupt transitions were seen in the same fibre from normality to severe disease There was multiplication of the nuclei of the sarcolemma, with many mitotic figures, many were surrounded by granular basophil cytoplasm The capillaries were crowded with polymorphs and some eosinophils, a few escaping into the surrounding tissue (fig 5) Some macrophages and normal numbers of mast cells were present There was no increase in collagen, and the reticulin frame work was normal The few vessels and nerve bundles seen appeared normal No motor end-plates were found in specially impregnated portions, a not unusual finding in a randomly selected biopsy (Woolf 1954)

Histochemistry—The histochemistry of normal muscle is reviewed by Dempsey et al (1946) and by Roskin (1952) In the present case there was complete loss of glycogen from diseased fibres and almost complete loss from normal fibres (Best's carmine stain) The weak beta metachromasia (Schmorl's thionin) of normal fibres in frozen section was absent from degenerate fibres, possibly owing to the loss of phosphorus compounds found in various myopathies (Nevin 1934) Staining with Fettrot 7B or with Sudan black B in propylene glycol, and with Nile blue, revealed no abnormality apart from absence of I band staining with Sudan black in fibres which had lost their striation Baker's acid hæmatin showed that the phosphatides were increased and uniformly distributed in the diseased fibres Similarly, acetone Sudan black (Berenbaum 1954) showed an increase in the bound lipids of these fibres These findings are of interest because the deposition of lipid in muscle is increased after denervation (Artom Friedlander et al 1941) and in vitamin E deficiency lis and Spencer 1936) No acid fast pigment, a charac feature of vitamin E deficiency in animals (Mason ford 1947) was present Small calcium deposits were seen in the most degenerate areas (cf Paul 1924) No ferric iron was found Azo-dye coupling methods (Pearse 1953) showed only traces of acid and alkaline phosphatases confined to vessels Dempsey et al (1946), who claimed to have found phosphatase in muscle fibres, exposed their sections to substrate for 24–72 hours, ample time for the production of artefacts, used Gomori's (1941) method, now well known to produce misleading pictures (Pearse 1953) Esterases were shown by the method of Nachlas and Seligman (1949) of incubating 37°C at pH 7 4 for 40 minutes, with alpha naphthyl acetate as the substrate Numerous esterase positive bodies were seen, evidently corresponding to the cytoplasm of proliferating sarcolemmal cells (fig 6) No myoneural junctions were seen Although some cholinesterase is associated with sarcolemmal nuclei and the sarcoplasm (Portugalov and Yakovlev 19 sarcolemmal cytoplasm is not normally stained by the technique Staining was unaffected by sodium taurocholate (5×10^{-3}M) Owing to unavoidable circumstances the effects of other differential enzyme-inhibitors were tested on tissues kept at –20°C for two days By this time any remaining enzyme activity was so low that the results were equivocal and the esterase could not be more precisely characterised Pickworth's benzidine stain showed patchy or complete loss of myoglobin from diseased fibres

Polarisation Microscopy—In paraffin sections the unaffected fibres were normally birefringent Here and there, an otherwise normal fibre showed an accumulation of granular intensely birefringent material along its edges The grossly abnormal fibres either consisted entirely of such material were optically inactive (fig 7) Insertion of a quartz first order purple plate (I wave length retardation) between, at 45° to, polariser and analyser gave a picture similar to that obtained by Matoltsy and his colleagues (Matoltsy Gerendás 1947, Gerendás and Matoltsy 1947, Gerendás et al 1947) during the extraction of actin and myosin from muscle and by Aloisi et al (1952) in rabbits with vitamin E deficiency In normal fibres the positively birefringent A bands were blue alternating with I bands of the same purple colour as the background In mildly affected fibres some of the I bands were negatively birefringent, varying from yellow to red, whereas the alternating A bands showed reduced birefringence More severely affected fibres showed progressive of striation, and replacement by yellow, orange, or granular and negatively birefringent material. The severely affected fibres were optically inactive Matoltsy his school consider that such changes are due to loss of positively birefringent actomyosin and the unmasking of negatively birefringent "N protein" Aloisi et al (19 however, think they are explained by loss of myosin depolymerisation and molecular rearrangement of actin.

Discussion

uscular Dystrophy

In 7 cases of paroxysmal myoglobinuria (not included the 15 listed above) muscular dystrophy was diagnosed inically or muscle atrophy supervened (Meyer Betz 911 Louw and Nielsen 1944 Scherwin 1945 Wissler 948, Kreutzer et al 1948, Acheson and McAlpine 1953 ipp and Shukers 1955) It has been suggested that aroxysmal myoglobinuria is simply an acute manifestaion of muscular dystrophy However muscle dystrophy as not supervened in some cases followed up for fifteen r sixteen years (communication of R Debré to Acheson and McAlpine 1953 and of R Hed to Elek and Anderson 1953) No muscle atrophy resulted from fifty attacks in seven years in the case published by Spaet et al (1954)

The specific histological features of muscular dystrophy are hypertrophy great variation in size and longitudinal splitting of muscle fibres, followed by fatty infiltration (Adams et al. 1953) In no case of paroxysmal myoglobinuria studied histologically were these features seen although muscular dystrophy cannot thereby be excluded

The appearance of myoglobinuria in muscular dystrophy is not surprising The renal threshold for myoglobin is 15–20 mg per ml of plasma (Yuile and Clarke 1941) only a fifth of that of hæmoglobin Myoglobinuria may therefore be caused by any sufficiently extensive and acute muscle damage A rough calculation shows that in an adult visible myoglobinuria may result from the destruction of about 200 g of muscle Myoglobin has consequently been found in the urine as a result of air raid injury (Bywaters and Beall 1941 Bywaters et al 1941) physical assault (de Langen 1946) electric shock (Fischer and Rossier 1947) gangrene due to arterial thrombosis (Bywaters and Stead 1945) and even it is claimed, severe exertion in healthy people (Ono 1953)

It may be presumed that in muscular dystrophy, muscle damage may progress sufficiently rapidly to cause myoglobinuria However this cannot be taken to mean that muscular dystrophy is the cause of every unexplained case of myoglobinuria where there is no supporting clinical or familial evidence

Carbohydrate Metabolism

Suggestions that paroxysmal myoglobinuria may be due to faulty metabolism of carbohydrate have been largely based on a supposed analogy to equine myoglobinuria (Carlström 1931) In Hed's (1947) cases attacks occurred on a low-carbohydrate diet, and glucose lerance curves were abnormal Abnormal curves and lycosuria have been noted in myotonic dystrophy Morgulis and Spencer 1930) but not in progressive uscular dystrophy (Tyler and Perkoff 1951) In the esent case renal glycosuria was the only relevant bnormality Disturbances of carbohydrate metabolism re possibly more the effect than the cause of the muscle isorder

ossibility of Abnormal Myoglobin

Several types of human hæmoglobin exist many of hich are a cause of disease (White and Beaven 1954) his fact suggests that an abnormal myoglobin may be cause of paroxysmal myoglobinuria The existence of fœtal type of myoglobin is suggested by the fact that yoglobins of fœtal and adult origins differ in extract bility from tissues (Björck 1949) in solubility (Jonxis nd Wadman 1952) and in light absorption (Rossi anelli et al 1951) A myoglobin relatively insoluble in he reduced state is suggested by the analogy of the bnormal hæmoglobin of sickle cell anæmia (Perutz and Mitchison 1950 Perutz et al 1951) Simple solubility elationships are unlikely to apply in the muscle cell argely occupied by organised protein structures and evere exertion or other factors may induce changes in oxygen tension pH &c., sufficient to render an abnormal myoglobin insoluble and incapable of carrying on its function of short term storage of oxygen (Millikan 1937 1939 Lawrie 1952) Theorell and de Duve (1947) found that the myoglobin in the urine in a case of paroxysmal myoglobinuria differed slightly from normal myoglobin in the shape of the crystals, light absorption and solubility Although these workers discounted these differences, we think they are at least suggestive and worthy of further investigation

The same considerations apply to the other proteins of muscle but knowledge of these is so rudimentary that even speculation about their rôle in this disease is unwarranted at present

The finding of increased red-cell fragility in the present case also found by Hed (1953) in 1 of his cases suggests that examination of all the hæm pigments in these patients might be rewarding

Summary

A case of paroxysmal myoglobinuria of unknown ætiology is described Myoglobin was found in the urine by spectroscopy and by crystallisation. For the detection of myoglobinuria we recommend conversion to carboxy compounds

Muscle biopsy showed severe degenerative changes the accumulation of an esterase in the sarcolemmal cells and the appearance of negative anisotropy during degeneration of fibres

The myoglobin content of the diseased muscle was much reduced.

14 previously published cases of myoglobinuria without another associated muscle disease are collected of which 5 were fatal. 7 additional cases were associated with muscular dystrophy

The ætiology is unknown We suggest that an abnormal myoglobin may be present

Many colleagues have helped in the study of this case Our thanks are due to Dr H Loewenthal senior pathologist Chase Farm Hospital, Dr R G Parrish, of the Royal Institution and Prof B K Johnson of the Imperial College of Science for much advice Prof W D Wright for permission to use the spectrophotometer Dr P Bauwens, of St Thomas's Hospital for electromyography and Mr R Smith, B.Sc Mr H Day and Mr E Siddle for technical help Mr H. Knight made the photographs Dr Leonard Crome and Dr H. Loewenthal translated several papers.

REFERENCES

Acheson, D , McAlpine D (1953) *Lancet* ii 372
Adams R D , Denny Brown, D Pearson C. M (1953) Diseases of Muscle. London
Aloisi, M., Ascenzi A Bonetti, E. (1952) *J Path. Bact* 64 321
— — — (1954) *Ibid* 67 475
Artom C. (1941) *J biol Chem* 139, 953
Berenbaum M. C (1954) *Nature Lond* 174 190
Beznák, M (1948) *Acta chem. scand* 2 333
Bielschowsky, M., Green H N (1943) *Lancet* ii 153
Björck G (1949) *Acta med scand* 133, suppl 226
Bowen W J (1948) *J biol Chem.* 176 747
Buchanan D Steiner P E. (1951) *Arch. Neurol Psychiat* 66 107
Bywaters, E. G L. Beall, D (1941) *Brit med J* i, 427
— Delory G E. Rimington, C Smiles J (1941) *Biochem J* 35, 1164
— Dible J H (1943) *J Path Bact* 55 7
— Stead J K (1945) *Clin Sci* 5 195
Carlström B (1931) *Skand Arch. Physiol* 61 101 *Ibid* 62 1
Debré, R., Gernez C., Sée G (1934) *Bull Soc méd Hôp Paris* 50 1640
de Duve C (1948) *Acta chem scand* 2, [illegible]
de Langen, C D (1946) *Acta med. scand* 124 213
Dempsey E. W Wislocki, G B., Singer M (1946) *Anat Rec* 96 221
Eggleton, M G (1944) *Lancet* ii, [illegible]
Elek S D Anderson H F (1953) *Brit med J* ii 533
Fischer H Rossier P H (194) *Helv med. acta* 14 212.
Friedlander H D Perlman I Chaikoff I L. (1941) *Amer J Physiol* 132 24
Gerendás M Matoltsy A G (1947) *Hung acta physiol* 1 [illegible] 129
— Szarvas, I., Matoltsy A G (194) *Ibid* p 121
Gomori G (1941) *Arch. Path* 32 189
Green H N (1943) *Lancet* ii 14
— Stoner H B, Bielschowsky M (1949) *J Path Bact* 61 101
Günther H (1924) *Virchows Arch* 251 141
Hed R (1947) *Nord Med* 35 1586
— (1953) *Arch. intern Med.* 92 [illegible]
Hipp H R., Shukers C F (1955) *Ann intern Med* 42 187

References continued overleaf

SPINAL CORD DAMAGE BY EFOCAINE

EDWIN CLARKE
M D Durh , M D Chicago, M R C P
LECTURER IN NEUROLOGY
ROBERT MORRISON
M.D Edin , F R C S E , F F R
CONSULTANT RADIOTHERAPIST, MEDICAL RESEARCH COUNCIL RADIOTHERAPY RESEARCH UNIT
HILDA ROBERTS
M R C S , F.F A R C S , D A , D C H
LECTURER IN ANÆSTHETICS
POSTGRADUATE MEDICAL SCHOOL OF LONDON AND HAMMERSMITH HOSPITAL

EVER since the introduction of cocaine as an anæsthetic agent (Koller 1884), attempts have been made to improve regional anæsthetics One that is long acting and has been introduced recently is 'Efocaine,' a solution of procaine (1%), procaine hydrochloride (0 25%), and butyl aminobenzoate (5%) in polythylene glycol mol wt 300 (2%), propylene glycol (78%), and water It has been recommended for intercostal and paravertebral block, for anorectal and peri-incisional infiltration, for musculoskeletal disorders, and for various minor operations Extensive use has been made of it and at first excellent results were reported (Iason and Shaftel 1952, Ansbro et al 1952, Deaton and Bradshaw 1953), although unpleasant after-effects were occasionally observed (Bonica 1952)

Since then, however, it has become increasingly evident that efocaine is far from satisfactory (*British Medical Journal* 1954), and several serious and occasionally fatal accidents have followed its use The case reported here illustrates these unfortunate sequelæ, although previous experience with the drug had been favourable

Case-report

An accountant, aged 64, was admitted on June 4, 1954

Eleven years previously, in 1943, he underwent a total laryngectomy for laryngeal neoplasm. He remained in good health until December, 1952, when he developed a carcinoma of anaplastic type in the region of the uvula Treatment was given with teleradium and he remained well for a further year until he developed a recurrence in the glands of the neck and in the pharyngeal region A further course of radiotherapy was begun with the patient attending as an outpatient Soon, however, he complained of pain in the interscapular region, radiating to the front of the chest and having the characteristics of root pain In spite of the usual analgesics this became so severe that he had to be admitted to hospital.

On admission his general condition was poor He spoke with an œsophageal voice and had an efficient tracheostomy An enlarged mobile gland 3 cm in diameter was present on the left side of the neck, and laryngoscopy showed an ulcerated carcinoma in the lower pharyngeal region The nervous and other systems were normal, apart from local tenderness in the upper thoracic region of the spine

Biopsy of the lymph gland showed infiltration by anaplastic squamous carcinoma Radiography of the thoracic spine showed no abnormality An electrocardiogram (E.C.G) was typical of posterior myocardial infarction

Operation for Relief of Pain

Under the influence of the radiotherapy the pharyngeal tumour and the enlarged gland underwent resolution, but the pain, which seemed to involve T2–T4 bilaterally, persisted, and large amounts of morphine were necessary to subdue it The patient was a very anxious and sensitive person and reacted excessively to his symptoms The relationship of the pain and the E C G findings was difficult to assess, and it was considered that despite the lack of radiological proof, spinal metastases with root involvement were probably the cause of the pain

To control this symptom a paravertebral block was suggested, and it was done on the left side first in order to assess the effect before doing it on the right On July 28 efocaine 3 ml was deposited around T3, T4, and T5 roots on the left. The operation was uneventful, but about ten mintues later the patient suddenly collapsed, with very low blood pressure, gasping and shallow respirations, and loss of consciousness. Intravenous nikethamide and a saline infusion were given and within two hours he had made an almost complete recovery , but damage to the spinal cord was now obvious

Spinal Cord Lesion

A partial Brown Séquard syndrome was present, with almost complete paralysis of the left leg and a sensory level at T3 The back pain was much less severe Treatment with an indwelling catheter, tidal drainage, and physiotherapy to the legs was begun at once An infection of the bladder responded to antibiotics, and three weeks later voluntary micturition was possible The control of bowel function which had also been affected, much improved Simultaneously the legs improved, and six weeks after the onset of symptoms the patient could walk a few steps with the aid of a walking machine The back pains had not returned, and he needed no analgesics

His progress, however gradually became slower, and about ten weeks after the paravertebral injections his condition began to deteriorate His legs became weaker , he could no longer stand or walk , and the sensory impairment was more obvious An enlarged lymph node was found in his neck. Sphincteric disturbances returned, and a bladder infection supervened Further radiographs of the thoracic spine were still normal Both motor and sensory paraplegia was now complete, and he died on Nov 27, 1954 six months after admission and four months after the paravertebral block.

Post mortem Findings

There were secondary deposits of carcinoma in lymph nodes of the neck, thyroid gland, and lungs Coronary occlusion with an old infarction of the posterior wall of the left ventricle, and bilateral bronchopneumonia were found together with bilateral pyelonephritis, acute cystitis and gangrene of the perineum

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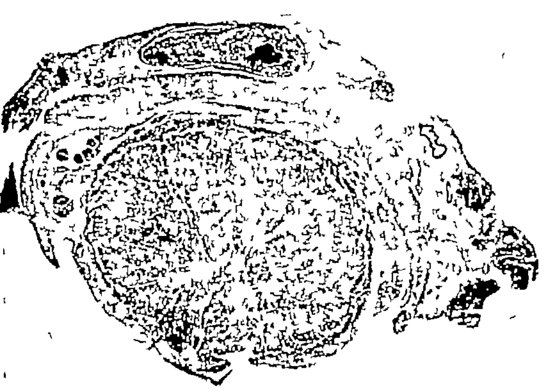
DR BERENBAUM AND OTHERS REFERENCES—*continued*

Hittmair, A (1925) *Wien klin Wschr* 38 431
Huber, J Florand J Lièvre, J A , Neret Mme (1938) *Bull Soc méd Hôp Paris*, 54 725
Jonxis J H P Wadman S K (1952) *Nature Lond* 169 884
Kovách A G B , Bagdy D Balázs R Antoni F Gergely, J Menyhárt, J , Iranyi M , Kovach, E (1952) *Acta physiol hung* 3, 331
Kreutzer, F L , Strait, L Kerr, W J Hrenoff M K (1948) *Arch intern Med* 81 249
Lawrie R A. (1951) *Nature, Lond* 167, 802
— (1952) *Ibid*, 170 122
Louw A , Nielsen H E (1944) *Acta med scand* 117 424
Mason K E Telford, I R (1947) *Arch Path* 43 363
Matoltsy A G , Gerendás, M (1947) *Nature, Lond* 159 502, *Hung acta physiol* 1 116
Meyer Betz F (1911) *Dtsch Arch klin Med* 101 85
Millikan G A (1937) *Proc roy Soc* B 123 218
— (1939) *Physiol Rev* 19 503
Morgulis, S , Spencer, H C (1936) *J Nutr* 12 173
Nachlas M M , Seligman A M (1949) *Anat Rec* 105 677
Nevin, S (1934) *Brain*, 57, 239
Ono, I (1953) *Tohoku J exp Med* 57 273
Paul, F (1924) *Wien Arch inn Med* 7, 531
Pearse A G E (1953) Histochemistry Theoretical and Applied London
Perri G L Gorini P (1952) *Brit J exp Path* 33 440
Perutz M F , Liquori, A M , Eirich, F (1951) *Nature Lond* 167, 929
— Mitchison J M (1950) *Ibid* 166 677
Portugalov B B Yakovlev, B A (1951) *C R Acad Sci U R.S.S* 78, 5, cited by Roskin (1952)
Rees M W (1949) Cited by Kendrew in Roughton F J W , Kendrew J C Hæmoglobin London
Roskin G I (1952) *Adv mod Biol Moscow*, 34, 268
Rossi Fanelli, A (1948) *Science* 108 15
— (1949) *In* Roughton F J W Kendrew J C Hæmoglobin London
— Cavallini D , De Marco C (1954) *Arch Biochem* 50 496
Schaar, F L La Bree, J W Gleason D F (1949) *J Lab clin Med* 34 1744
Scherwin, J (1945) *Nord Med* 25 460
Shenk, J H , Hall, J L , King, H H (1934) *J biol Chem* 105 741
Spaet T M Rosenthal M C Dameshek W (1954) *Blood* 9 881
Stokes W (1953) Cited by Acheson and McAlpine (1953)
Theorell H (1932) *Biochem Z* 252 1
— de Duve C (1947) *Arch Biochem* 12 113
Tyler F H Perkoff G T (1951) *Arch intern Med* 88, 175
Watson R H (1935) *Biochem J* 29 2114
White, J C Beaven G H (1954) *J clin Path* 7 175
Wissler H (1948) *Helv pædiat acta* 3 334
A L (1954) Communication to 88th Meeting of Pathological
iety of Great Britain and Ireland
W D (1954) *Acta Optica* 1 102
L Clark W F (1941) *J exp Med* 74, 187



Transverse section of spinal cord and meninges at T3 showing meningeal reaction thickening of dura mater and neoplastic deposits in epidural fibrous tissue mostly on posterior surface.

In the epidural space at T2 T3 and T4 was a mass of brownish fibrous material covering mainly the left and posterior surfaces of the dural tube It was 1 cm. thick at T3 and compressed the spinal cord Microscopy of this region revealed disorganisation of the cord meningeal reaction, thickening of the dura mater and invasion of the epidural fibrous tissue by clumps of neoplastic cells (see figure) Tumour cells were present in the vertebral bodies of T1–T9 invading the posterior longitudinal ligament at T3

Comment

Despite the difficulties caused by the presence of two aetiological agents in this case the close relationship between the paravertebral injection and the lesion in the spinal cord is indisputable The thickening of the dura and some of the cord changes no doubt resulted from the injection The deterioration after a period of recovery was probably due to lymphatic spread of the malignant tissue in the epidural space; if this had not occurred considerable improvement in the spinal cord could have been expected In view of the persistently normal radiographs it is difficult to ascribe the initial back pain to involvement of the vertebræ Microscopy however showed that extension from the vertebral body of T3 into the epidural space had taken place

Discussion

Like many other workers we had previously found efocaine an efficient means of producing caudal block to control intractable pain resulting from inoperable carcinoma of the uterus or cervix Although leg weakness developed in 1 of 7 such patients extension of the disease was probably responsible for this

Previous Reports

We have now found 20 reports of spinal-cord damage produced by efocaine With our case the total is 21 but no doubt others have remained unpublished

Among the 14 recorded in detail there are 7 in which the efocaine was placed (often under direct vision) around intercostal nerves at the level of the transverse processes usually to combat postoperative pain (Shapiro and Norman 1953 case 1 Nowill et al 1953a, case 2 Brittingham et al 1954 cases 2 and 3 Berg 1954 Griffith 1954 Knight and Luth 1954) A paravertebral block was done in 6 (David 1953 Nowill et al 1953a; Brittingham et al. 1954 case 1 Hubbard 1954 our case) and the patient of Angerer et al (1953) had an intercostal nerve block

All the patients developed some degree of dysfunction of the spinal cord either immediately (as in our case) after some hours, or (as in case 2 of Brittingham et al 1954) after as long as two days An episode of acute shock such as occurred in our patient, has been reported only once (Angerer et al 1953) Details of the neurological findings are not always available but 4 patients had a complete and 7 an incomplete transverse lesion of the cord 5 of the latter had a type of Brown Séquard syndrome Death took place in 5 cases but in only 2 (Angerer et al 1953 David 1953) was it due directly to the efocaine in the 3 others (Brittingham et al 1954 Berg 1954 and our case) the primary condition for which efocaine had been used produced or contributed to the fatal outcome. Of the 9 known survivors 2 recovered well and were the only ones to walk again 4 improved slightly and 3 did not improve Those less severely affected were more likely to show recovery but the speed of onset of symptoms of the spinal lesion did not seem to influence the outcome

3 patients came to necropsy but in 2 cases (Brittingham et al 1954 case 1; Berg 1954) full details are not given In the patient who developed symptoms and signs of a spinal lesion after an intercostal nerve block in the posterior axillary line thrombosis of an intercostal vein and artery was found (Angerer et al 1953) There was widespread necrosis and acute inflammation of the spinal cord In our case the necropsy appearances were complicated by neoplastic invasion of the epidural space There is no doubt, however, that the epidural fibrous tissue and some of the disorganisation of the cord resulted from the paravertebral injection of efocaine

Method of Production of Damage by Efocaine

During a paravertebral injection the following possibilities of damaging the cord exist

(1) Introduction of the efocaine into the cord or subarachnoid space as has happened with alcohol (Molitch and Wilson 1931 Hirschboeck and Gillespie 1942 Mandl 1947) The presence of efocaine in the cerebrospinal fluid however does not necessarily indicate that this has taken place for Angerer et al (1953) found procaine in the cerebrospinal fluid although the efocaine was injected at least 8 cm. lateral to the spinal canal

(2) Injection of efocaine directly into the epidural space or near by so that it can readily find its way into it

(3) The case of Angerer et al. (1953) suggests that involvement of intercostal veins and arteries may occasionally cause damage to the cord

(4) Moore (1953) and Moore et al. (1954) have shown satisfactorily that efocaine injected into an intercostal nerve of a monkey can travel centrally by way of the perineural spaces of the nerves and roots to reach the parenchyma of the cord and damage it in some cases

It seems likely that any one or more of these mechanisms may take place and the second or the fourth probably is responsible for the present case

Effect of Efocaine on Nervous Tissue

Damage to peripheral nerves (Bonica 1952 David 1953) and other structures (Hubbard 1954 Knight and Luth 1954) has occurred in man and Margolis et al (1953) have produced it experimentally in various animals Mannheimer et al (1954) show that the effect of efocaine on a peripheral nerve is comparable to that produced by section The solvent vehicles in efocaine (propylene glycol and polythylene glycol mol wt 300) necrotise animal tissues (Maykut and Ryan 1953 Fabre et al 1953 Mannheimer et al 1954) and Nowill et al

(1953b) have confirmed this in man These substances are responsible for the long lasting anæsthetic effect of efocaine, but they produce their effect by destroying rather than anæsthetising tissues There can be little doubt that these suspending agents rather than the anæsthetics are the offending constituents of efocaine, and the benzyl alcohol in 'Symprocaine,' which has also damaged the cord (Panter 1953), probably plays the same rôle That efocaine is not always destructive is shown by our previous cases , but, in view of its deleterious effects in some people, it should not be brought into contact with peripheral nerves, roots, or spinal cord, and it would probably be wise to discontinue its use altogether

Summary and Conclusions

A case in which the spinal cord was damaged by paravertebral injection of 'Efocaine' is described, and 20 others are cited

In this preparation the anæsthetic agents are dissolved or suspended in vehicles capable of destroying tissues with which they are left in contact

Efocaine can damage nervous tissue severely, and when injected near the spine it may travel via nerves and spinal roots to the spinal cord to produce severe destruction

Its value as a regional anæsthetic is in question, and its use should probably be abandoned

REFERENCES

Angorer A L Su H H , Head, J R (1953) *J Amer med As*
153 550

Ansbro F P Iason A H Shaftel H E Halpern A., Latter
F S Bodell B (1952) *Anesthesiology*, **13**, 306

Berg R (1954) Cited by Moore (1954)

Bonica J J (1952) *J Amer med Ass* **150** 1581

British Medical Journal (1954) i 926

Brittingham T E Berlin, L N Wolff H G (1954) *J Amer
med Ass* **154** 329

David L J (1953) Cited by Moore (1953)

Deaton W R jun , Bradshaw, H H (1953) *Surg Gynec. Obstet*
97 140

Fabre J Boymond P , Riotton G Bonstein, I (1953) *Praxis*
42, 1014

Griffith C A (1954) Cited by Moore (1954)

Hirschboeck, F J Gillespie, M. G (1942) *Arch Neurol Psychiat
Chicago* 48 320

Hubbard, S T (1954) Cited by Moore (1954)

Iason A H Shaftel H E (1952) *Amer J Surg* 83 549

Knight R T , Luth D V (1954) Cited by Moore (1954)

Koller, C (1884) *Klin Mbl Augenheilk* **22**, suppl p 60

Mandl F (1947) Paravertebral Block in Diagnosis, Prognosis and
Therapy Minor Sympathetic Surgery London p 35

Mannheimer W Pizzolato, P Adriani J (1954) *J Amer med As*
154, 29

Margolis G Hall H E Nowill W K. (1953) *Arch Surg* 67, 15

Maykut, M. O Ryan E A (1953) *Canad med. Ass J* 69, 419

Molitch M Wilson G (1931) *J Amer med Ass* 97 247

Moore, D C (1953) *West J Surg Obstet Gynec* **61**, 635

— (1954) *Surgery* **35**, 109

— Hain R F , Ward A Bridenbaugh, L D jun (1954)
J Amer med Ass **156**, 1050

Nowill W K Hall H Stephen C R (1953a) *Arch Surg* 67 13

— — Margolis G (1953b) *Ibid* p 731

Panter K (1953) *Zbl Chir* **78**, 1153

Shapiro S K Norman D D (1953) *J Amer med Ass* **152**, 60

Preliminary Communication

MAIZE AND PELLAGRA

MICROBIOLOGICAL and chemical evidence indicates that almost all the nicotinic acid in cereals, such as maize, wheat, barley, rye, and rice, is present in an alkali labile, " bound " form, that differs from the known nicotinoyl derivatives and is only partially utilised by *Lactobacillus arabinosus* and *Lb casei* [1] Hydrolysis with 0 5 N NaOH or strong mineral acids liberates the nicotinic acid which is then available to bacteria The " bound " form of nicotinic acid, present in maize and other cereals, does not appear to serve as a source of the vitamin for the nicotinic-acid-deficient rat [2,3] and chick [4,5] Experiments with pigs in which a deficiency of nicotinic acid had been produced on diets containing a large proportion of maize [6,7] indicate, by implication, that the " bound " form is equally unavailable to the pig There is no direct evidence about its availability or otherwise to man

The full biological activity of nicotinic acid for the rat can be released by hydrolysis with 0 5 N-NaOH,[2,3] but again the availability to man of such products is uncertain It was felt that experiments on the pig might help in answering this point, in view of the similarity of its nicotinic acid metabolism to that of man [9] The results are briefly reported here A full account of this work will be submitted for publication elsewhere

EXPERIMENTAL

Eighteen weanling pigs of both sexes, weighing 37–59 lb , from four litters were assigned to three groups In the preliminary stage of the experiment, a deficiency of nicotinic acid was induced in all groups by giving a maize diet similar to that of Chick et al ,[8,9] and consisting of ground white maize 79, pea meal 10 5, purified casein 5, cod-liver oil 3 salt mixture 2 5 When the pigs ceased gaining or lost weight they were put on the experiment proper group 1 (deficient controls) was maintained on the deficient diet, modified by replacing the maize with maize reconstituted from its milling fractions , group 2 (positive controls) received, in addition to this modified diet, 6 mg nicotinic acid daily , group 3 was given a diet in which the milling fractions of maize—namely, bran and hominy meal—containing most of the aleurone layer and 73% of the total nicotinic acid, had been hydrolysed for 30 minutes with 0 5 N NaOH to liberate " bound " nicotinic acid The pigs were maintained on these diets for 9 weeks or until they succumbed to deficiency They were weighed twice weekly and their daily food intake was recorded The free and " bound " forms of nicotinic acid present in the diets were determined microbiologically [10] and chromatographically [11] Tryptophan was estimated chemically [12]

RESULTS AND DISCUSSION

Preliminary Deficiency Period —Seventeen pigs became deficient within 17–63 days One animal, which had been assigned at the beginning of the experiment to group 3, did not become deficient during the period of the experiment and was therefore not included It became deficient only in the 14th week and was killed in a moribund condition for post-mortem examination

Experiment Proper —The seventeen deficient pigs in the three groups were given, over a period of 9 weeks their experimental diets The average weight gains of the three groups are shown in the accompanying figure The average weight of the deficient pigs (group 1) did not increase , two animals finished the experiment in a moribund state and two others died in the 4th and 5th weeks The remaining two pigs completed the experiment without showing signs of deficiency Both required an exceptionally long preliminary period, 59 and 63 days before they ceased to grow One of them resumed growth shortly thereafter , the other at first lost weight but recovered towards the end of the experiment Such a recovery has been observed by other workers [6,7] All the pigs supplemented with 6 mg nicotinic acid daily (group 2) recovered from the deficiency and maintained a steady gain in weight The pigs given the alkali hydrolysed maize fraction (group 3) recovered also and gained in weight, though at a slower rate than the animals of group 2 which received the nicotinic acid supplement

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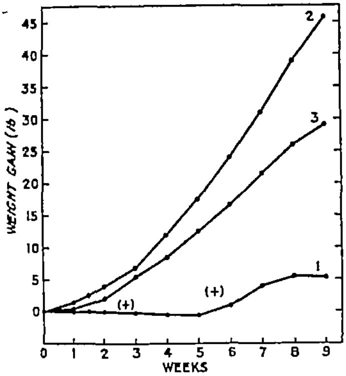
1 See review, Kodicek E *Ann Rep chem Soc* 1951 48 290
2 Chaudhuri, D K Kodicek E *Biochem J* 1950, **47**, xxxiv
3 Kodicek, E *Ibid* 1951, 48 viii
4 Krehl W A , Elvehjem C A , Strong, F M *J biol Chem* 1944 **156**, 13
5 Coates, M E , Ford, J E Harrison, G F , Kon S K , Shepheard, E E Wilby F W *Brit J Nutr* 1952 6 75
6 Birch, T W Chick H Martin C J *Biochem J* 1937, 31 2065
7 Braude, R. Kon, S K White, E G *Ibid*, 1946 40 843
8 Chick, H Macrae, T F , Martin, A J P , Martin C J *Ibid* 1938, **32**, 10
9 Chick, H , Macrae T F Martin, A J P , Martin C J *Ibid*,

10 Clegg K M., Kodicek, E Mistry, S P *Ibid* 1951 50 326
11 Kodicek, E Reddi K K *Nature Lond* 1951, 168 475
12 Graham, C E Smith, E P , Hier, S W , Klein D *J biol Chem* 1947, 168 711



Average weight-gain of pigs deficient in nicotinic acid receiving various treatments.

1 Group 1 deficient controls.
2 Group 2, positive controls, receiving 6 mg nicotinic acid daily
3 Group 3 receiving alkali-treated maize fraction.
(+) Death of animal

The average weight gains intake of food of nicotinic acid and of tryptophan are given in the table It will be seen that the control pigs lost some weight that the other two groups gained appreciably and that they also ate much more food and that these differences were statistically significant

Pigs of group 2 that received nicotinic acid grew significantly better than those of group 3 on hydrolysed maize they also ate more but this difference was not statistically significant. The deficient group 1 consumed on the average 7 7 mg daily of nicotinic acid of which only 0·8 mg was considered to be available The vitamin supplemented group 2 had 20 8 mg total nicotinic acid daily of which 7 6 mg was available Group 3 on the diet in which 73% of the nicotinic acid present in maize had been liberated by alkaline hydrolysis, had daily 9 6 mg nicotinic acid in free form out of a total of 12 6 mg It thus appears that the recovery of the pigs in group 3 was correlated with the availability of nicotinic acid as found previously in rats [illegible] The curative action of the hydrolysed maize diet given to group 3 was in striking contrast to the pellagra producing action of the untreated maize diet given to the same pigs in the preliminary deficiency period when they consumed about the same amount (10·8 mg) of nicotinic acid but almost all in 'bound form We conclude therefore, that the main factor responsible for the recovery of the pigs in group 3 was the availability of free nicotinic acid We cannot however exclude as a contributory factor some other changes in the bran and hominy meal fractions which may have occurred during the relatively mild alkaline hydrolysis That there may have been some alteration in other constituents—e.g in the proportion of amino acids [13]—is indicated by the fact that the pigs of group 3 though they consumed more free nicotinic acid than the vitamin supplemented group 2 did not do as well as the latter

EFFECT OF ALKALINE HYDROLYSIS OF MAIZE FRACTIONS (BRAN AND HOMINY MEAL) ON THE AVAILABILITY OF NICOTINIC ACID FROM MAIZE TO DEFICIENT PIGS

(Average weight gain intake of food nicotinic acid and tryptophan calculated for a period of 9 weeks)

Group	Diet	No of pigs	Weight gain (lb per week)	Food intake (lb per week)	Intake of nicotinic acid (mg per day)		Intake of tryptophan (g per day)
					Free	Bound	
1	Deficient	6	−0 2 ± 1 26	1 3 ± 0 32	0 8	6 9	0 8
2	+ nicotinic acid 6 mg per day	6	5·0 ± 0 33	[illegible] 5 ± 0 15	7 6	13	1 5
3	Hydrolysed maize fraction	5	3 [illegible] ± 0 02	2 1 ± 0 17	9 6	3·0	1 3

Standard error

As pigs react to a deficiency of nicotinic acid in many ways similarly to man, it is possible that the following considerations apply to both species

(1) If the 'bound" nicotinic acid is not available to man, the only factor that determines the pellagra preventive potency of a cereal would be its tryptophan content, and *possibly its ability to alter by its own* amino acid content the imbalance of amino acids in the diet [13] Thus there is in these circumstances no need to postulate a toxic factor in maize to explain its pellagra producing properties

(2) The daily requirement of man has been estimated, on the basis of the average intake in the diet to be 12 mg nicotinic acid [14] In this value is included the ' bound ' *nicotinic acid in cereals that may amount to about* 30–50% of the total nicotinic acid intake from an ordinary diet If the bound nicotinic acid is not available the above estimate of the daily requirement will be too high and should be reduced An amount of 6–8 mg daily seems a more appropriate estimate This value agrees well with the curative doses of yeast which were needed by Goldberger and Tanner [15] to cure pellagrins.

(3) Alkaline treatment which liberates the ' bound nicotinic acid in cereals could be a possible way of enrichment of the foodstuff In this connection treatment of maize with lime water has been reported to cure nicotinic acid deficiency in rats [16 17] and it has been suggested that lime water treatment of maize as practised in Mexico may be responsible for the low incidence of pellagra among maize-eaters in that country However this mitigating effect of treatment with lime water has not been observed in other laboratories for both the rat [18] and man [19] The explanation of these discrepancies has to await further experiments.

Dame Harriette Chick and the late Sir Charles Martin took a keen interest in this work and we derived much benefit from talks and discussions with them. The experiments would not have been possible without the generous assistance we received from Quaker Oats Ltd Southall, Middlesex who carried out the large scale hydrolysis and preparation of the maize fractions We are particularly grateful to Mr B C L. Summers and Mr J J Holt of that company for their willing help We wish also to thank Mr P Wilson for technical assistance

R Braude
Ph.D Reading
S K Kon
D Sc. Reading
Ph.D Warsaw F R I C
National Institute for Research in Dairying,
University of Reading
K G Mitchell
B.Sc., Ph D Reading
Dunn Nutritional Laboratory
University of Cambridge and
Medical Research Council
E Kodicek
M D Prague Ph D Camb

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13 Koeppe, O J Henderson L M *J Nutr* 1955 55 23
14 Kodicek, E. *Lancet* 191 1 380
15 Goldberger J., Tanner W F *Publ. Hlth Rep Wash* 1925 40 54
16 Laguna, J Carpenter K J *J Nutr* 1951 45 21
17 Cravioto, R O Massieu, G H Cravioto O Y Figueroa F de M *Ibid* 1952 48 453
18 Krehl W E Henderson, L. M. Huerga J De la Elvehjem C A. *J biol Chem* 1946 166 531
19 Goldsmith G A Gibbens, J Rosenthal, H L. Unglaub W G., Miller O N *Fed Proc* 1954 13 458

Medical Societies

ROYAL SOCIETY OF MEDICINE

Intraventricular Administration of Drugs

ON April 19 the section of psychiatry, with Dr W MAYER-GROSS, the president, in the chair, had the opportunity of hearing, from colleagues in other disciplines, about some recent work on the injection of drugs into the ventricular system of the brain

IN THE CAT

Dr W S FELDBERG, F R S, described, as a physiologist, the method he and Dr S L SHERWOOD use with cats, and showed a film illustrating some of their results Drugs injected into the lateral ventricles, he said, come into contact with the important masses of grey matter lying round the third ventricle and the aqueduct

In this study the injections were made into the ventricles of conscious cats The method first used was to bore a hole through the cat's skull, under general anæsthesia, and allow the skin to heal over it, injections could then be made through the skin But the method was frightening, the cats struggled, and had to be restrained, and the person making the injection had no confidence that he was in the lateral ventricle rather than the surrounding brain tissue Moreover, the cats soon became hostile A 'Polythene' covered cannula has therefore been devised which can be implanted at operation, screwed into the skull and left in position It is closed at the top by a rubber diaphragm, and injections can be made through this without annoying the cat—which is held gently in position by an assistant

The film showed the operation for implanting the cannula in an anæsthetised cat, the normal behaviour of the recovered animal, and radiographs of the skull with the cannula in position Cats tolerate the cannulas well, and some have had them implanted for over a year

The effects of various drugs were also shown After *acetylcholine* the cat retched, gave a few cries, and then sat still and subdued until the effects wore off After *atropine* the same cat became lively, and appeared to be enjoying itself, rolling on its back or pacing and prancing Its appraisal of its surroundings, however, seemed to be impaired, for it ignored a hand stretched out to it—though before the injection it had played readily with the assistant's hand, reaching up to it with its paws and head With larger doses of atropine it retched and vomited, its breathing became rapid, and its nictitating membranes relaxed and spread partly across the eyes

Under *adrenaline* or *noradrenaline* the cat became completely relaxed, drowsy, and flabby—laid out, as though under pentobarbitone ('Nembutal') With methantheline ('Banthine') there was also retching, vomiting, and rapid respiration The cat used in this experiment was unable to stand or walk and developed nystagmus while under the influence of the drug, even though this was given in doses which would have had no effect if given intravenously *Tubocurarine* produced salivation, defæcation, much plaintive crying, and finally convulsions—which were checked by giving intraperitoneal pentobarbitone This cat, in spite of its experiences, was very friendly on recovery from the drug, and appeared to have forgotten the whole episode—in contrast to the cats in the original experiments, which long remembered resentfully attempts at injection

A very lively cat was chosen for injection with the *anticholinesterase* drug, di isopropylfluorophosphonate (D F P) After the injection it at once began licking and scratching itself as though afflicted with violent irritation over its body and head, but the delayed effect of the drug was to put the cat into catatonic stupor during which it would retain for as long as ten minutes any posture into which it was put It was perfectly capable of normal movement, however, for when it had remained for some time balanced across the stretchers of an upturned stool, a gentle push from behind caused it to jump down in its usual well coördinated manner

Dr Feldberg believes that these are central effects, not due to any considerable absorption of the drugs into the [illegible] circulation for atropine, when injected intra[illegible]y, has no effect on the pupillary reflex, and tubocurarine produces convulsions instead of the paralysis seen when it is given subcutaneously Retching and vomiting followed the injection of many drugs, no doubt because they are all injected into the same region, but otherwise the variety of symptoms produced is considerable, including drowsiness, convulsions, catatonia impaired awareness, sleep, muscular incoordination, and spastic paralysis The scratching and licking after D.F.P is also a central, not a peripheral, effect, for the same behaviour can be produced by electrical stimulation of the midbrain The pruritus produced by morphine may be of similar origin, and so may the itching of lichen planus, which is relieved dramatically by the removal of a few millilitres of cerebrospinal fluid (C S F) at lumbar puncture D F P produces catatonia resembling that seen in schizophrenia This drug has been tried in the treatment of patients with myasthenia gravis, but has been given up because they complained of insomnia and terrifying nightmares and hallucinations Given to schizophrenics, it was found to exacerbate the psychosis Accumulation of acetylcholine in the midbrain may perhaps be responsible for clinical catatonia Some of the drug actions studied may be an imitation of actions occurring normally in the brain tissue round the third and fourth ventricles

Dr S L SHERWOOD had begun intraventricular experiments after exploring the electrophysiological aspects of this work in W S McCulloch's laboratory in the Illinois Neuropsychiatric-Institute, and he is now working with Dr Feldberg He has studied the response to various drugs in 26 psychotic patients of long standing Their ages ranged from 20 to 47 and their psychosis had persisted for periods of three to twenty three years, and 20 of them were schizophrenic, 7 had been leucotomised before the drug injections were started, 7 had leucotomy after the study had begun, and 8 had no surgical treatment In each case the cannula was introduced into the lateral ventricle by the same technique as that used in the cats, and electroencephalographic and other observations were made on the effects of different drugs

Adrenaline was tried in 5 patients, 4 of them with catatonia and 1 with epilepsy, the drug produced general relaxation and lowering of muscle tone, the rigid patients letting their heads sink back on the pillow There was no paralysis In 3 patients there were flushing, sweating, nausea, and vomiting and all became drowsy within ten to thirty minutes, though they were easily roused Those who had been inaccessible responded to simple questions, and one who had not spoken for years remarked "I wish someone would do this to you, doctor" The effects wore off two to three hours later, leaving them as they had been before the injection except for some slight increase in spontaneity

The results of *atropine* (3 cases) were inconclusive, but spontaneous movements of a relaxed kind increased, and the patients showed a readiness—quite unusual—to smile and giggle Methantheline was given to 11 patients (9 cases of catatonia, 1 of paranoid, and 1 of simple schizophrenia), an hour later they were all more active than they had been Given large doses they became overactive, and showed signs of distress so that the drug had to be stopped They described hallucinations and delusions, and while some of them were aware of the abnormality of these experiences, they did not lose them Under the influence of the drug, Dr Sherwood noted their complexions improved *Cholinesterase* was tried in 15 cases, but it was difficult to get enough of the drug in a pure condition most early preparations caused nausea and vomiting and a fall of blood pressure The best source proved to be a soluble preparation from human red cells, and preparations made from this were less toxic Within a few minutes of the injection the patients flushed and became more accessible and after two to three hours they had improved sufficiently to look after their personal needs in 6, indeed behaviour approached normal In one this improvement has persisted for four years and in another for two, both had been leucotomised before receiving this treatment All patients became more alert and coöperative, but 2 became agitated—perhaps because of increased awareness

On the effects of *hyaluronidase* both alone and with other drugs, no definite conclusions were reached.

Serotonin was given to 4 patients. Within a few minutes they began to yawn and clear their throats they flushed and then paled and sometimes vomited They began to talk freely—one sang and shouted—though there seemed to be no change in their thought processes Still they were more pliable more interested and cleaner One was able to go home for three months.

Some of the responses seen—such as vomiting, a fall of blood pressure and of C.S F pressure, and improvement of complexion—were common to many drugs Some women with amenorrhœa began to menstruate again He emphasised the suitability of intraventricular injection as a tool for the study of mental illness

Dr DEREK RICHTER commented on the value of interdisciplinary collaboration it cannot be often that a neurosurgeon and a physiologist have worked together He was impressed by the extent of the field opening for research and looked forward to still wider collaboration Perhaps a competent psychologist could add to the value of experiments such as this by assessing animal behaviour—for instance by the use of animals trained in mazes In cats licking and washing is perhaps a frustration symptom it is hard to understand it It would be interesting to study the effects of the hallucinogens by this method In the past decade we have recognised that the different brain centres differ in biochemistry and this method should add to our knowledge of their metabolism

Mr R H J WATSON described some results of feeding anticholinesterase to rats in order to reduce their cholinesterase level He has measured their behaviour in terms of their capacity before and after to solve problems and he has noted that it is more difficult to extinguish conditioned responses in them after feeding than before He compared this with the greater difficulty of extinguishing such responses in introverted, as compared with extraverted people In the deeply introverted schizophrenic extraverting drugs such as cholinesterase might be expected to produce improvement

The CHAIRMAN asked why, when the circumventricular brain substance already contains more adrenaline than other parts of the brain, the injection of adrenaline should have a sedating effect Dr FELDBERG replied that a substance like adrenaline which occurs naturally in the body presumably needs to be released into a form in which it can act he cited the case of the action of acetylcholine in a sympathetic ganglion

New Inventions

A LABOUR-WARD BED FOR SAFER ANÆSTHESIA

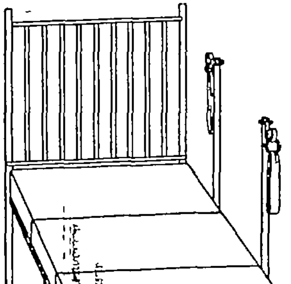
THE dangers associated with the inhalation of stomach contents during anæsthesia in obstetric practice have recently received considerable attention and there are many factors which make obstetrical anæsthesia specially hazardous In one respect patients who are anæsthetised on a labour ward bed are at a special disadvantage because there is not usually any mechanism for rapidly lowering the head Some obstetric beds do have a tilting-device, but at best it is of a type that involves delay in operation and during this delay vomit may be inhaled The proper management of regurgitation of stomach contents under anæsthesia is to recognise it immediately and immediately to lower the head so that postural treatment has been adopted before the vomit can be inhaled Immediate recognition is a matter for the vigilance of the anæsthetist but it is no less essential that the mechanical device for changing the patient s posture shall operate at a moment s notice

The ordinary obstetric bed in use at Guy s Hospital is simply a wide bed with a solid top and fitted with staples on one side to receive lithotomy poles when the patient is anæsthetised in the cross bed position The tilting device here described has been adapted to this bed.

In the new bed the upper surface is divided into three equal sections. One side of the middle section pivots between the adjacent top and bottom sections, while the other side of the middle section is free to fall below the level of the other two sections thus giving the patient s whole trunk a head-down inclination when she is in the lithotomy position across the bed The normal horizontal position of the middle section is maintained by an extra leg which pivots freely on the side-bar of the middle section If it becomes necessary to tilt the patient a sharp kick on the pivoted leg sends it under the bed and the middle section immediately drops into a tilted position

The chief problem in design was to devise a pivoted leg which was rigid enough to prevent the unintentional collapse of the middle section yet free enough to yield instantly to an intentional but moderate push with the foot. Mr W P Bentley chief engineer Guy s Hospital solved the problem by suggesting a leg mounted on a wheel to which a foot brake is attached With the brake on there is sufficient friction between the rubber tyre of the wheel and the floor to prevent the leg from slipping in response to accidental pressure On the other hand a deliberate push on the foot-brake first releases the brake and then continues easily to displace the leg on its free-running wheel thus the middle section collapses immediately Two springs under the middle section help to cushion the sudden fall And bolts are provided to lock the middle section securely when the bed is in routine use with the unanæsthetised patient The mattress is, of course divided

This bed has been made by Mr F Woodall, of Guy s Hospital works department, and his ingenuity and craftsmanship have overcome many difficulties of detailed construction These constructional details will differ with different types of bed to which the principle may be applied It is my purpose now merely to draw attention to the principle of the device for immediately lowering the patient s head by a simple movement of the foot so that precious seconds are not wasted after the patient has vomited and so that the hands of the anæsthetist may be free for other urgent duties



Guy's Hospital
London, S E 1

G F GIBBERD

Reviews of Books

Fundamentals of Radiobiology

Z M BACQ, professor in the University of Liège, PETER ALEXANDER, Chester Beatty Research Institute, Institute of Cancer Research, London London Butterworths Scientific Publications New York Academic Press 1955 Pp 389 40*s*

RADIOBIOLOGY is concerned with the study of radiation effects on living matter It is a fairly new branch of science which has become very important since the release of nuclear energy Professor Bacq and Mr Alexander have written a fascinating and valuable survey based on the results of extensive research, scattered through 960 publications Besides presenting the physical and chemical aspects of radiation in an easy and understandable manner, the book offers useful information, not only to those engaged in fundamental research on radiobiological problems, but also to those using radiation with a practical aim

The chapter dealing with the pathological effects of radiation on biochemical functions is of special interest The authors draw attention to the fact that, except during the last days of life, little change is caused by sublethal doses of irradiation on general metabolism. The book summarises a great amount of experimental work on the processes by which normal physiological conditions can be re established after irradiation The practical aim of such investigations is to provide a scientific basis for the treatment of radiation victims

The difficulties met in the interpretation of complex reactions—e g, the rôle of adrenal hyperactivity and of the pituitary in radiation sickness—are indicated Clinicians in general, and radiotherapists in particular, will be interested in the section on chemical protection against X and γ radiation, which includes a discussion of the possible biochemical mechanism by which various substances protect from radiation injury There is a chapter about protection by shielding part of the body and by the injection of spleen and bone marrow homogenates The last chapter surveys the pathological effects of atomic explosions and gives a brief account of the genetical hazards of radioactivity

The book is well documented and illustrated and is written in a lively style Professor Bacq and Mr Alexander have made every effort to represent the selected material objectively, and their book will appeal to all who are working with radiation and are interested in radiobiological problems

Amphetamine in Clinical Medicine

Actions and Uses W R BETT, M R C S, F.R.S.L, LEONARD H. HOWELLS, B SC, M D, F.R C.P, physician, United Cardiff Hospitals, A D MACDONALD, M A, M D, M SC, Leech professor of materia medica, therapeutics, and pharmacology, University of Manchester Edinburgh and London E & S Livingstone. 1955 Pp 78 7*s* 6*d*

THIS well-produced little book "is intended merely as a guide to the general practitioner as to when and when not to employ this basically useful drug" The chapter headings show that amphetamine is most widely employed in borderline conditions between the physical and the psychiatric. Psychiatrists may feel that in such conditions as fatigue and depression, psychopathic states, and enuresis and behaviour disorders in children the psychological approach is more fruitful than the pharmacological Experience of alcoholism and other drug addictions, the subject of another chapter, shows that amphetamine may play a major rôle in maintaining such addictions The book is useful as a record of the conditions in which amphetamine has afforded opportunity for attempts at symptomatic treatment

Maladies de l'intestin et du péritoine

JEAN RACHET, ANDRÉ BUSSON, CHARLES DEBRAY Paris Flammarion 1954 Pp 1104 Fr 9400

THIS loose-leaf book is one of the series of modern French textbooks edited by Prof Pasteur Vallery-Radot and Prof Jean Hamburger The intention is to keep this [illegible] up to date by issuing yearly supplements and revisions In this volume Dr Rachet and his colleagues give a full account of diseases of the intestine, rectum, and peritoneum

In the first chapters major symptoms are discussed generally Detailed descriptions of individual diseases follow, with numerous references and illustrations Some of the latter are excellent, and indeed the whole production is extremely good To the English reader it may seem that undue emphasis is given to such matters as the size and position of the colon, since many physicians in this country attach little importance to ptosis of the colon or whether it is long or short On the other hand the account of intestinal gas is particularly good and not easily found in English textbooks The sprue conditions receive no more than 20 pages and the effects of wheat gluten in the diet in cœliac disease and steatorrhœa is only mentioned briefly

A number of uncommon diseases are included, but a few rare conditions such as Whipple's disease seem to have escaped notice The index is perhaps hardly as full as might be wished, but the orderly arrangement of the subject matter makes this a good book of reference

The Path Through Penguin City

HARRY R LILLIE, B SC, A M I C E, M B London Ernest Benn 1955 Pp 302 25*s*

As an engineer, biologist, and doctor, Dr Lillie covers a wide range of subjects in this book, but if his *Path Through Penguin City* is labyrinthic there is a guiding thread in his exhortation "Don't let us hate, but seek to help, that we may co-operate in brotherhood with all the creatures of the earth"

The book includes a full account of his commendable efforts towards promoting humane killing methods in whaling, interesting observations on the wild life of the Antarctic, reflections on the basic values of life, and a naturalist's excursions into theology In fable like conversations with him the penguins, gallant ambassadors of the whales, arraign man as the breaker of the peace of their realm He ends with a vision of Nature taking her revenge for the misdeeds wrought by man against his fellow creatures. Dr Lillie's colleagues may be disappointed that he has not told them more about his medical work in the Antarctic The drawings and photographs are from Dr Lillie's own pen and camera

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My Fight against Osteo-Arthritis (*London* Faber & Faber 1955 Pp 105 8*s* 6*d*)—This little Pilgrim's Progress describes how Eve Orme, attacked early by osteo arthritis of the hip, has come by painful stages to recognise and sum up her enemy, to face him squarely, and, with professional help, to parry or soften many of his blows For fellow patients the story and her reflections and practical advice should be most helpful Her medical advisers come out of the tale better than other healers Her best friend, found through a clinic, was a skilful and imaginative physiotherapist A wise, candid, tolerant, and friendly little book

Physical and Psychical Research (Reigate Omega *Press* 1954 *Pp* 213 15*s*)—Psychical research seems to have a fascination for some physicists, as famous names attest. Isaac Newton was the greatest of these parergal inquirers into "the more far flung regions of human experience and thought"—as Mr C C L Gregory and Miss Anita Kohsen, the authors of this book, call their paranormal field—but he was not the most fortunate in his choice of subject and method Mr Gregory and Miss Kohsen approach psychology, psycho analysis, and parapsychology with a sophisticated understanding of the modes of thought that prevail in the natural sciences and are usually considered essential for any scientific work They hold that we may be satisfied with knowledge derived by either logico deductive synthesis, inductive synthesis, operationalism, or intuition, subjects of inquiry such as dynamic psychopathology and psychical research which do not derive support from the second or third of these functions are in a weak position at present After covering a wide field in their review of the nature of belief and acceptable evidence, they plead for less scepticism and a loosening of the conceptual requirements of science, which should not, in their view, be necessarily self validating Though their argument is suggestive, they do not sufficiently consider the routes of error, so easily trodden when the traveller leaves the sanctioned highway

THE LANCET

LONDON SATURDAY APRIL 30 1955

Surgery of Temporal-lobe Epilepsy

HUGHLINGS JACKSON over seventy years ago suggested that certain epileptic phenomena in which the aura or the whole attack consisted in a dreamy state—often with semi purposive automatic movements, or ill-defined *hallucinations of smell or taste* or of epigastric sensation—reflect a discharging lesion in the temporal lobe. During the past decade this concept of "temporal lobe epilepsy" has been elaborated, largely with the help of more accurate electro-encephalographic techniques for localising the site of electrical discharge. The group of epilepsies so defined is often associated with personality disorders which may be grave, indeed it is becoming more and more likely that these are the cases that have given rise to the idea of the epileptic personality and epileptic deterioration. Furthermore as the number and range of anticonvulsant drugs has increased it has become clear that they are especially resistant to drug treatment, and sometimes when control of the fits is achieved, the personality disorder grows worse rather than better. The possibility of successful surgical treatment is therefore particularly worth exploring.

PENFIELD and FLANIGIN[1] in 1950 reported the results of excising the anterior part of one temporal lobe in which a recognisable macroscopic lesion was held to be causing fits: abolition or great reduction of attacks followed in over half of their 55 cases. BAILEY et al[2] in 1953 recorded considerable improvement both in fits and in associated psychiatric disorders in 42% of 64 patients, in many of whom the diagnosis was less definite in that no macroscopic lesion had been demonstrated though the general clinical picture and pattern of attacks and a localised electrical abnormality were regarded as sufficient indications for excision. In our last issue Mr MURRAY FALCONER and his colleagues summarised further encouraging results. Of 30 patients 27 had complete or considerable relief from fits, and of the 29 who had an associated personality disorder 20 showed improvement in this also. These workers emphasise that, as PENFIELD suggested, removal of the deeper structures of the lobe—the uncus, hippocampus, and amygdaloid complex—is desirable. They also make a small but important technical advance in endeavouring to remove the lobe in one piece, which offers far greater opportunity for histological study.

Both from these observations and from the number of cases now being treated surgically it is clear that the operation holds promise. Nevertheless very careful thought is needed before recommending any procedure that involves irreversible change to the brain, and we must know as certainly as possible what psychological changes it is likely to induce. After his temporal lobectomy on the dominant side FALCONER notes a slight nominal dysphasia in a third of his cases, and some impairment of verbal learning. How far these will be a disability must depend on the nature of the patient's life and work. Perhaps more important ultimately, however, are the finer personality changes that might follow—changes less likely to emerge in formal tests than to be seen by those living in intimate contact with the patient. At this stage we should take with a gram of salt any dogmatic statement that no such alterations occur, bearing in mind the earlier experiences with leucotomy, and the evident association between disorder of personality and lesions of the temporal lobe. We must also be certain that improvement is specifically due to removal of temporal lobe tissue which is behaving abnormally. There is a growing tendency to bare cortical excisions for epilepsy mainly on the site of localised electrical abnormality, but such abnormality may be transient nor need it necessarily be initiated at its site of cortical manifestation (GIBBS,[3] RUSSELL MEYERS[4]). Even at the morphological level, the causative association between the lesion and the epilepsy can be criticised, as is done by Dr CROME on p. 882. Such arguments cannot invalidate good clinical results of surgical treatment but they reinforce the demand for adequate clinical assessment over an adequate period. BAILEY et al[2] conclude their paper by saying that "no appraisal of the surgical treatment of epilepsy will have much validity unless at least five years have elapsed since operation in every case", and most people who are experienced in the management of epilepsy will welcome these cautious words.

The decision to operate will always have to be made on an individual judgment. In some cases the chance of even temporary improvement, especially where there is a serious personality disorder, will outweigh other considerations. But as it is at present unlikely that in this difficult field of treatment operation will be lightly withheld, the need is chiefly to temper enthusiasm. Those now engaged in this work are evidently well aware of the still unanswered questions it poses. Such teams as those of FALCONER and his colleagues from the Guy's Maudsley unit are particularly well qualified to answer them, and in doing so they will not only advance therapy but add to our knowledge of cerebral function.

Medical Education

OUR students get a vocational training in clinical medicine, preceded by a period of preparatory education in relevant basic sciences. The vocational training has become unsatisfactory because the student is confronted with more and more information and techniques which distract his attention from essentials; and the educational preparation has become unsatisfactory because from the earliest stage the student is taught a great deal that he has no need or wish to know. The earlier part of the curriculum ought to be more vocational[5] and the later part more educational: we should recognise that the attempt to be comprehensive is futile if it prevents comprehension; and we should urgently be seeking, for our students, a new balance between principles and practice which will make them better qualified to practise medicine as it is and will be Yet in Britain we have hardly made any progress towards doing these things

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[1] Penfield, W., Flanigin H. *Arch Neurol Psychiat Chicago* 1950 64 491

[2] Bailey P, Green, J R., Amador L., Gibbs F A *Proc Ass Res nerv Dis* 1953 31 341

[3] Gibbs F A. *Amer J Dis Child* 1954 88 596

[4] Meyers R. *Epilepsia* 1951 3 9

[5] O'Meara, R. A Q *Lancet* Jan. 29 1955 p 191

In the basic sciences which we teach, many changes have taken place[5], and these are well described by Dr D C SINCLAIR, demonstrator in human anatomy at Oxford, in a book on *Medical Students and Medical Sciences* [6] which could be read with advantage by clinical as well as preclinical teachers As they have grown, the basic subjects have been affected by what SIR RUSSELL BRAIN has called the " counter current of specialisation " and have become more intimately mixed with each other Anatomy, aided by radiology, is able to leave the cadaver and begin the study of living structure Physiology, which gave birth to biochemistry has now (as SINCLAIR points out) a child as big as itself, and it has also spread so far and wide that there is some doubt as to exactly what remains at the centre Moreover, though anatomy, physiology, and biochemistry are still the mainstay of the preclinical curriculum, biophysics and statistics are now with good reason beginning to be admitted Most people recognise, too, the need for future doctors to learn something of the development of the human mind and of its normal reactions, though this does not necessarily imply recognition of psychology as a science (SINCLAIR, as an anatomist suggests that medical students would perhaps learn all the psychology they need by watching general practitioners at work to which some psychologists and possibly many general practitioners might retort that the same process would teach the student all he is likely to remember of anatomy) As for morbid anatomy, which has so long (in Britain) been neither preclinical nor clinical, but a curriculum in itself, increasing knowledge of function and dysfunction shows that it can no longer be expected to provide all the answers The necropsy-room is still a palace of truth, but the truth it offers is not the whole truth

SINCLAIR has lately made a study of medical schools both in this country and in the United States, and all who have done likewise will agree with him that we have been relatively slow to translate the above changes into teaching practice Efforts have been made, especially in anatomy and physiology but, as he says, " there are still many schools where the formal lecture course deals in full textbook detail with the scientific side of Pathology, where the museum of gross specimens is the main feature of the teaching, where there is little liaison between clinicians and pathologists, and where the emphasis is on making the students into pathologists rather than on making them into doctors " (Indeed in some schools there is little liaison even between bacteriologists and morbid anatomists) In the United States there is at least much awareness that times have changed and that new problems of education cannot necessarily be solved by old methods Furthermore, American universities, themselves primarily responsible for maintaining the standard of their graduates, are free from external restrictions on their curricula and thus have the great advantage of freedom to experiment Many have made use of advantage, and in terms of changes in the preclinical curriculum, which in America includes pathology, two main aims are discernible

The first is to increase the integration of the basic sciences with each other, grouping them in time so that the student passes from study of normal structure and function to that of abnormal (In Western Reserve University the experiment of integrating the preclinical subjects with clinical work is in progress) Though the value of these experiments cannot yet be gauged, there is at any rate no doubt that any medical school in which the staff get together to plan a new and improved programme benefits greatly from the resultant integration of the teachers, irrespective of any changes that may or may not be made in the curriculum.

The second aim has been to correlate preclinical studies more closely with clinical work In many schools this goes well beyond the liaison between the departments of physiology and medicine which is customary in Britain and in some it seems indeed, to go beyond the limits set by the maturity of students in their first and senior years and by their lack of any clinical technical skill We should do well to study these schemes and note their practical difficulties, for they are attractive in principle and frequently advocated It should be remembered however, that one of the reasons for bringing clinical work into the preclinical period is to attract the student—to offer a clinical carrot to a preclinical donkey—and it seems preferable in principle to make basic sciences interesting and exciting in their own right, as they certainly can be It is also relevant that the student is increasingly confronted with science during the clinical part of his training, and now finds that he learns much physiology from the cardiologist and the neurologist just as he has always learnt surgical anatomy and surgical pathology from surgeons This natural evolution has been recognised in some schools in America, and at Johns Hopkins (the traditional home of basic sciences) only an introduction to physiology is given in the preclinical department, the remainder coming later from the staffs of the medical and surgical departments of physiology

Reorganisation of the curriculum is not a cure for all ills, and tinkering with it does more harm than good Yet in SINCLAIR's words, ' unless we are constantly thinking over how the form of our teaching could be made more stimulating and thus more valuable, it is fatally easy to slip into the comfortable bonds of routine, and to be satisfied that if the student complies with the statutory regulations of the medical degree we have done our best by him "

In the final analysis the most important factor in medical education will always be the attitude of mind of the teacher Since the late war there has been a shortage of preclinical teachers, and it is to be hoped that SINCLAIR is right in thinking that today " academic work in Britain is no longer quite the bad financial proposition relative to clinical work that it used to be, bearing in mind the many advantages of the quiet life " But unhappily the possession of the strongest team of basic scientists gives no guarantee of keen and able teachers " The Great Teacher," SINCLAIR aptly remarks, has been replaced by " The Great Research Worker ' and for many teaching is a " tedious activity " to be " performed in spare time " Similarly, for some clinicians teaching has come to be primarily a verbal by-product of the concomitant care of their patients, delivered to a group of unnamed students Yet the interest taken in his work by the student will always be a reflection of the interest taken in him as an individual by his teachers, and in this respect a contrast to our disadvantage has been drawn between British and American medical schools The American teacher, as a rule, is interested in the individual student and

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lon Oxford Medical Publications 1955 Pp 154 25s s no longer much interested in didactic teaching Above all (again in SINCLAIR's words) "he knows what he is trying to do, and how he intends to set about doing it" His objective if he is a preclinical teacher in any of the better schools is not to impart factual knowledge but rather to inculcate a scientific method of thought and to stimulate the student to use this so that he may learn for himself, and remain able to learn for himself Such an objective is attainable for a large proportion of students but only if examinations are not exerting on them a diametrically opposed incentive It is for this reason that in the best American schools examinations now play a very small part in the lives of students—a sharp contrast with the recent past Such examinations as remain are intended principally to augment education rather than to assess knowledge and they are no longer the main factor in deciding what the student tries to learn. Surely the time has come when we in this country should open our eyes both to the imperfections of our teaching and to possible means of removing them?

Annotations

ALBERT EINSTEIN

Einstein was one of the greatest scientists of all time Some would say that with Newton he stood above them all.

He was born in Ulm on March 14 1879, of Jewish parents. As a boy he does not seem to have made a favourable impression on his teachers—probably because of his dislike of the ordinary school discipline, his shyness, and his great desire for privacy But those who were nearer to him discovered his love of music and his promise of creative ability It is said that at an early age he learned almost unaided to solve simple algebraical problems, and that he discovered for himself a proof of the theorem of Pythagoras. There is the story that when given a mariner's compass at 5 years of age he showed profound emotion and wonder at the sight of the needle pointing for no apparent reason always in the same direction One might almost suppose that at that moment there came to his childish mind some vague foreshadowing of his life's great work—his abolition of the absolute attributes of space and time and his creation of a space time geometry which while it successfully embraced the phenomena of gravitation never fully succeeded in including those of electricity and magnetism

From 17 to 21 Einstein was a student at the Zürich Polytechnic and a year later he became a Swiss citizen and obtained a quite humble job in the Swiss Patent Office at Berne This gave him the leisure he required for developing his thoughts In his first year at Berne he began to produce papers on theoretical physics while in his third year 1905 he published three papers which fairly shook the scientific world One of these dealt with the Brownian movement manifested by microscopic particles as a result of molecular bombardment and paved the way for the only really direct proof of the existence of molecules Another was concerned with the photo electric effect and involved a completely revolutionary advance in Planck's quantum theory The third was a 30 page paper giving the full development of his Special Theory of Relativity As a result of these achievements he held between 1909 and 1913 professorships in Zürich and Prague; and in 1914 he went to Berlin as professor of physics and director of the Kaiser Wilhelm Institute for Research During these years he had been working on an extension of his Special Theory and finally after many failures and disappointments, he published in 1915 his greatest masterpiece, the Generalised Theory of Relativity—his theory of gravitation

In 1933 Einstein left Berlin as a result of the Hitler purge and after spending some months on the Continent, emigrated to the United States where he became a professor of physics at the Institute for Advanced Studies in Princeton There up to the time of his death he was occupied in trying to develop a further extension of his theory which would embrace the electromagnetic as well as the gravitational field. But though he believed that he had obtained partial success, the complete solution always eluded him About 1940 he became an American citizen

It is often supposed that Einstein's greatness lay in his mathematical ability That was not so Though he was judged by the highest standards, a fine mathematician there were others even in his own generation who were much greater His surpassing brilliance was in the field of theoretical physics and his stupendous imagination and piercing insight enabled him to probe its foundations to discover the flaws which were there and to rebuild from the very bottom the whole structure anew To do this he had to employ the most complex mathematical machinery but that machinery was not of his own making It had been developed by others—by Gauss Minkowski Riemann Ricci and Levi Civita

It is remarkable that many of the fundamental conceptions he put forward during the development of his theories are essentially simple—so simple that generations of thinkers had passed them by without appreciating their significance The idea of the absolute simultaneity of separated events had passed unchallenged since the days of Newton Yet Einstein saw that in terms of physically possible observations the idea was meaningless, and that the difficulty could be over-come only by completely changing our ideas on space and time This he did and then went on to develop his Special Theory of Relativity Again at the outset of his work on the Generalised Theory he was struck by the curious coincidence that the inertial mass and the gravitational mass were always proportional to one another This fact together with the similarity between the effects of a gravitational field and those of an accelerated coördinate system suggested to him that there were strong a priori reasons for supposing that an extension of his theory to include accelerated motions might be achieved if the manifestations of gravitation could be shown to arise out of the peculiar geometrical properties of space time Although in both these cases a vast labour lay between the first idea and the developed theory the ultimate victory could scarcely have been achieved without these flashes of inspiration of which there were many more examples

It has been said that if Einstein had never written a word on Relativity he would still have been one of the foremost theoretical physicists of his generation his revolutionary contributions to the quantum theory in its earlier phases would have sufficed to ensure that The greatest bugbear of modern science is its dual character Microscopic physics has to be expressed in terms of quantum theory which depends on laws of probability while macroscopic physics has to be expressed in terms of relativistic theory which is governed by the laws of causality And the two theories appear completely incompatible Most scientists believe that ultimately when the two become merged into one the underlying theory will be of the probability type, while the relativistic theory for large scale phenomena will be found to be derivable from it statistically Einstein took the opposite view He felt that the probabilities uncertainties and discontinuities of the quantum theory while providing a useful tool in the present incomplete state of knowledge was fundamentally unsatisfactory and represented only a passing phase in science He felt that the all-embracing theory would be found to be based on the laws of causality And it was his belief that the first step towards this larger synthesis was a further extension of his Generalised Relativity which would embrace in a space-time geometry not only gravitation but electromagnetism

In spite of his retiring nature Einstein played a leading part in the general affairs of the world in which he lived He was an outspoken and courageous pacifist, and during the first world war he was one of the few German intellectuals who refused to sign a manifesto in support of German militarism instead he issued one of his own protesting against it In later years he vigorously opposed Hitler and Nazism and their anti-Jewish activities, and it was in support of his fellow Jews that he thrust aside his shyness and made the few public appearances of his career

SUCROSURIA

ONCE sucrose is absorbed into the blood-stream it is not metabolised but excreted in the urine But sucrose is not a reducing sugar and so will not be detected in the urine by routine chemical examination Reports of patients with sucrosuria are very rare In 1939 Elmer et al [1] described a single patient and reviewed earlier reports They concluded that there were two varieties of the condition in adults in "endogenous" sucrosuria, which has been noted in patients with pancreatic disorder, the sucrosuria persists even though sucrose is absent from the diet, and in "exogenous" sucrosuria, as in their own patient, sucrose in the diet is either poorly converted to glucose and fructose in the intestine or is absorbed unsplit by the gut wall

Infants and small children are less tolerant of sucrose than adults, and Lahdensuu [2] showed by tolerance tests that the intestinal absorption of sucrose, and hence sucrosuria, is increased by feeding sodium bicarbonate and lessened by feeding hydrochloric acid In 1910 Reuss [3] had noted that sucrosuria was common in infants who had had gastro enteritis, and this he attributed to increased permeability of the intestinal wall Obviously, therefore, the significance of sucrosuria in infants and young children must be carefully evaluated Moncrieff and Wilkinson [4] quote paper-chromatography observations by Woolf that not more than 30 mg per 100 ml of urine is found after meals in normal infants and children Any considerable amount of sucrose in infants and children, therefore, is likely to mean an anomaly either of sucrose digestion or of intestinal permeability Reiner and Weiner [5] described a 7-month-old boy who had temporary sucrosuria during a febrile illness At the age of 18 months the boy was mentally defective Moncrieff and Wilkinson [4] have recorded three cases—a girl of 30 months, a girl of 18 months, and a boy of 18 months—in which sucrosuria up to 150 mg per 100 ml was present on a normal diet All three children were mentally defective and had hiatus hernia These children excreted sucrose, lactose, fructose, and occasionally glucose in abnormal amounts when fed sucrose and lactose, but sugar excretion was normal when they were given glucose, fructose, and lactose Sucrose, with glucose and fructose, caused only a slight increase in glucose excretion It appeared, then, that it was lactose and sucrose together in the diet which caused the abnormal increase of urinary sugars Moncrieff and Wilkinson believe that the anomaly is one of intestinal absorption, since there must be some splitting of sucrose to explain the appearance of glucose and fructose in the urine after a test dose of sucrose They were unable to get any specimens of intestinal juice during life, but in one child a post mortem specimen was found to split sucrose and lactose The hiatus hernia, though perhaps part of the syndrome, cannot be the cause of the sucrosuria, for a number of children with such hernia were found to have normal sugar metabolism Again, it is tempting to attribute the mental defect to the sucrose in the blood, but in the one child who died the brain showed a number of developmental abnormalities

This is an interesting new field of study, not only for its clinical significance, but for the light it may throw on sucrose tolerance in normal infants and children

AORTIC STENOSIS

SURGICAL treatment of aortic stenosis [1,2] has quickly followed the successful relief of pure pulmonary stenosis, but the indications for operation are not yet defined. Bergeron and his colleagues [3] have recently analysed 100 cases of aortic stenosis to see whether the severity of the lesion and its prognosis could be predicted from clinical findings alone In all cases the diagnosis was confirmed at necropsy, and associated valvular lesions excluded, while three grades of stenosis—mild, moderate, and severe—were recognised from post-mortem measurements Bergeron et al conclude that assessment of the severity of the lesion from clinical findings is unreliable and difficult, for the severity did not necessarily match the signs except when they found the classical picture of systolic murmur and thrill, diminished second sound, and a small pulse, which almost always indicated severe stenosis Conversely, severe stenosis could be present with a systolic murmur alone, which was sometimes apical rather than basal In 11 cases, only 2 of which had mild stenosis, no murmur was heard at any time, which added to the difficulties in diagnosis, this was not just a terminal event due to extremely low output, since 2 patients only were in failure The second sound was unreliable as a guide to diagnosis or severity, but a pulse pressure of 30 mm Hg or less usually indicated severe or moderate stenosis, but severe stenosis was not ruled out by higher pressures Many patients remain symptom-free throughout their life or for many years. On the other hand, the onset of auricular fibrillation, heart failure, cardiac pain, or syncope were grave prognostic signs in Bergeron's series, for 75% of those in whom fibrillation developed, and 50% of those whose hearts failed, died within a year If two or more of these manifestations coexisted the prognosis was much worse But for most patients the outlook was good, and the mean age of death in the series was nearly 69

These findings agree with those in other series [4,5] and emphasise the many points of similarity between pure aortic and pulmonary stenosis, particularly as regards the murmur and second sound, and the long survival without symptoms in many cases This is not surprising since the two lesions are anatomically rather similar, and they both cause simple obstruction to the outflow from their respective ventricles At present the reasons why a ventricle should suddenly fail after overcoming an extra load for so long are imperfectly understood, although inadequate blood-supply to the myocardium from associated coronary narrowing or the stenosis itself must be important factors It is therefore impossible to judge when failure is imminent until symptoms have appeared. Campbell [6] has pointed out that a considerably raised right ventricular pressure in pulmonary stenosis may be an indication of the need for operation, even in the absence

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[1] Elmer A W, Krasowska M, Ptaszek, L *Acta med scand* 1939, 101 596
[2] Lahdensuu, S. *Ann Med intern Fenn* 1947, 36 293
[3] Reuss A *Wien klin Wschr* 1910, 23 123
[4] Moncrieff A, Wilkinson R. H *Acta pædiat, Stockh* 1954 no 100, p 495
[5] Weiner S B *Amer J Dis Child* 1939 57, 590

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[1] Bailey, C P Bolton H E, Jamieson, W L Nichols H T *Circulation* 1954 9, 22
[2] Logan A, Turner R *Lancet* 1951 i 1091
[3] Bergeron, J, Abelmann, W H, Vazquez Milan H, Ellis, L B *Arch intern Med* 1954 94 911
[4] Kumpe C W Bean, W B *Medicine* 1948, 27 139
[5] Lewes D *Brit med J* 1951 i 211
[6] Campbell, M *Brit Heart J* 1954, 16, 273

of symptoms; but in aortic stenosis right heart catheterisation cannot measure left ventricular pressure Whatever the final view on the right time for operation in aortic stenosis, all the evidence points to a rapid downhill course when major symptoms appear, and there is always the slight risk of sudden death without warning

SPENDING ON HEALTH

A CONCERN for health rather than ill health is seemingly a hard thing for a health service to achieve Prof Thomas McKeown speaking at the Royal Sanitary Institute s congress this week pointed out that not only the public but members of Parliament think that the health of the country depends mainly on the adequacy of the medical service and especially on the hospitals yet this view is not based on examination of the evidence There is a deep rooted reluctance among us to admit we cannot pay for everything that might conceivably help a sick person but if we go on trying to develop the medical services along traditional lines it will cost far more than we can afford Is there for instance any prospect of creating a satisfactory service for the mentally sick and the aged and chronic sick at a price which we shall be able to pay ?

The value of a medical service in Professor McKeown s opinion can be measured reasonably precisely in terms of mortality and morbidity rates and one way of judging the effectiveness of medical measures would be to discover the degree in which at a given cost they contribute to the extension of life or to making life more free from illness This cannot be done at some given moment once and for all what is needed is continuous appraisal such as is practised in any large industry which has to relate its affairs to changing conditions In any case the curative services he holds have contributed relatively little to the falling mortality and morbidity of the past 150 years the decline can be much more probably attributed to an improvement in living conditions, possibly influenced to a small extent by medical teaching Indeed it is not so much what happens when we become ill that matters we owe our longer healthier lives to the fact that in general we become ill less often Our hopes for the future then he thinks, should be vested largely in the prevention of disease, because that has been the main source of improvement in the past He does not suggest however that the preventive methods which have so far been successful if merely extended would serve to deal effectively with modern problems: in fact, he declares they will not Thus traditional methods may still reduce infant mortality in areas where it remains high but they cannot affect infant deaths due to congenital malformations or to prematurity—problems calling for a kind of research not traditionally regarded as in the field of public health Similar considerations apply he suggests to mortality in general: preventive medicine in fact should no longer be linked in our minds only with infectious diseases It must take within its scope the whole of human disease and must cease to think of bacteriology as its parent discipline

BLAND-SUTTON

John Bland Sutton was a great man—great enough to achieve distinction despite the opposition that blocked the progress of the pioneer He was born on April 1 a hundred years ago and it is fitting that his centenary should have been commemorated at the Middlesex Hospital and Medical School where he spent the whole of his professional life He was the first graduate of the school to be appointed a member of the honorary staff and of the many outstanding men who have been associated with the hospital he is perhaps the one who has endeared himself the most and whose influence has been greatest. It was his gift of the Bland Sutton Institute of Pathology since emulated at many other hospitals, that opened the way to the scientific development which has enabled the Middlesex to reach its prominent position among teaching schools The extent of the advance stemming from his inspired gift was well shown by the scientific exhibits presented in the Medical School on April 22 to illustrate the work now in progress. His original institute, to which are now added three others—the Barnato Joel Physics Laboratories the Courtauld Institute of Biochemistry, and the Institute of Clinical Research—together with six other professional departments arranged such a display as would have made him very proud But the exhibit which probably attracted most attention was the collection of Suttoniana which showed him as a man the diversity of his interests and above all, his humanity

Many still very much among us worked with Bland Sutton in the prime of his life, and three of the most distinguished Sir Gordon Gordon Taylor Sir William Gilliatt and Lord Webb Johnson, gave reminiscent addresses Bland Sutton was a man of Napoleonic mien and of the same assurance and he made his way with equal determination Choosing surgery at the start of his career he approached it by the customary path of the dissecting room and the post mortem room, but it was his genius to add the mortuary of the London Zoo It was experience in the latter that gave him the knowledge of comparative anatomy and pathology which contributed so much to his scientific eminence In this respect, and in the diversity of his interests he must have resembled John Hunter more closely than any surgeon since He was as great a surgeon as he was a man certain in approach as only an anatomist can be dextrous and unbelievably quick—the tip of his knife seemed as sensitive as the tip of a finger He was the first at any rate in England to excise a duodenal ulcer, the first to make a thoraco abdominal approach and the first to perform a hysterectomy for fibroids—a proceeding that raised a storm of protest Although he abhorred the idea that he might be thought a gynæcologist he was best known for his work in the pelvis He raised pelvic surgery to a new level and created a school of pelvic surgery Victor Bonney and Comyns Berkeley were his pupils

Bland Sutton is fast becoming a legend and like so many legendary figures he is surrounded by stories which illustrate the breadth of his character They are kindly stories for he was much loved A woman on whom he had operated later had occasion to consult another surgeon about a different problem An X ray film then showed half a needle embedded in the abdominal wall The patient chanced to see the film and when she seemed troubled the surgeon was quick to assure her that the needle was not the cause of her symptoms. That s not what I m worrying about ' she replied It s Sir John please don t tell him he d be so concerned

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Dr EGBERT MORLAND, editor of THE LANCET from 1937 to 1944, died on April 26 at the age of 80

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Special Articles

FUNCTIONAL SYMPTOMS IN ORGANIC DISEASE*

A. BARHAM CARTER
M.D. Camb., M.R.C.P., D.P.M.
PHYSICIAN, ASHFORD HOSPITAL, MIDDLESEX; ADVISER IN NEUROLOGY TO THE WAR OFFICE

It is hard enough to learn to distinguish the organic symptoms one from the other and to evaluate their importance; it is still harder to distinguish the organic from the functional. But these tasks are as nothing compared with the problem of the patient with an organic illness who produces functional symptoms which may modify and mask the progress of the underlying disease. This kind of case gives rise to more errors of diagnosis among good doctors than any other. Because it is rarely recognised as a problem in the teaching hospitals, the student is not prepared for the possibilities that will confront him in his practice; and even wide experience is often fallacious.

A clear definition of the word "functional" is necessary. It is here used to describe only symptoms produced by the emotional response of each patient to his illness, and is not used, as some authors use it, to describe organic and psychoneurotic symptoms of a similar type which interfere with the physiological functioning of the body. This latter use of the word can unfortunately be made to embrace so many general symptoms, such as dyspnœa, insomnia, and dyspepsia, that its original clarity of meaning becomes obscured. Whether "functional" is the best descriptive term for psychoneurotic symptoms associated with organic illness may be debatable; what is more certain is that most doctors know exactly what is meant by the phrase "functional overlay," and it seems more sensible to use words in their generally accepted meaning than to restrict their use to their original etymological definition.

What produces this difficult combination of symptoms? I think there are two main factors. First, this type of symptom may be due to a constitutional inability to accept or deal with the illness or its consequences. Secondly, it may be due to the effects of organic illness on a normal, or only slightly vulnerable, personality. A long, painful, recurrent illness, perhaps not well understood or managed by the doctor, may break the patient's morale. Ill-advised discussions at the bedside may start a train of obscure symptoms. Illness may bring domestic or financial changes which make the patient's attempts at adjustment almost impossible.

A functional symptom may appear at any stage of the illness, though often it shows itself as a prolongation of an organic symptom. It tends to appear suddenly and dramatically, but it is usually connected in the patient's mind with the original illness. This makes it all the more difficult to diagnose. I will now describe some examples in detail.

MOTOR DISTURBANCES

Aphonia

In patients with acute laryngitis the loss of voice may continue beyond the expected time of recovery. In organic illness it is fair to call this a functional symptom, though it is only the perpetuation of the symptom of the organic disease. It is always painless and is fairly easy to diagnose because:

(1) The patient can cough normally, though he is apparently unable to phonate.

(2) On inspection the cords show adductor paralysis on attempted phonation, with normal movements otherwise.

(3) Electric stimulation to the front of the neck will produce normal phonation.

Treatment is by active strong suggestion, stimulating the back of the throat, and making the patient phonate by gagging. This is usually one of the easiest and most satisfactory symptoms to treat.

Vomiting

In my experience this functional symptom arises only in the hysterical personality, and is not connected with the anxiety factor of organic illness. So far all my patients with this symptom have been women, and the illnesses have been of a relapsing nature, such as peptic ulceration, ulcerative colitis, rheumatoid arthritis, and sometimes pregnancy (though perhaps I should not describe this as an organic relapsing illness). It is also seen after abdominal operations and may be very troublesome.

This type of vomiting does not interfere with appetite, is effortless, and is unaccompanied by nausea. There is very little dehydration and no weight loss, though the patient will tell you "I bring everything up after every meal." Absence of ketosis, despite the vomiting, is another point; and if you watch the patient vomiting you will find no pallor, sweating, or tachycardia. It will often be surprisingly difficult to obtain a specimen for examination. Presumably only part of each meal is vomited, and the obvious well-being of the patient often makes diagnosis easy. It is of the utmost importance to make sure that you are not dealing with pyloric stenosis, cerebral tumour, or uræmia.

Treatment is difficult. Starvation usually helps, but I often find myself saying: "Your vomiting does not matter because you appear to be in good health in spite of it, and your stomach will adjust itself once you start work." I am careful not to ask them whether they have been sick.

Pyrexia

If a patient with an illness such as pulmonary tuberculosis, subacute rheumatism, or simple respiratory infection continues to have fever long after other signs have disappeared, the possibility of artificially produced pyrexia will arise. Needless to say, *it is unwise to make this diagnosis until one is sure that it is correct.*

Significant points are a grossly swinging temperature out of all proportion to pulse-rate, sweating, and colour, a continued fever with a persistently normal sedimentation-rate, and a fall in the temperature when taken under strict observation.

The pitfalls are latent pulmonary tuberculosis with a normal sedimentation-rate, drug fever, anæmia, and carcinoma, particularly hypernephroma. My own opinion is that these people are malingerers, and that all the grosser forms are due to radiators, hot-water bottles, hot drinks, and friction of the thermometer bulb; but I must admit that in some cases I have not found the explanation. The only treatment needed is to say that the temperature does not matter. So far all my cases in this group have been nurses.

Paralysis

Paralysis usually occurs after injury or during an epidemic of poliomyelitis. The traumatic cases are often associated with desire for compensation or fear of incapacity, and the infective cases with straightforward terror of the disease itself. In compensation cases the paralysis does not clear up at once after satisfactory settlement, unless the patient is malingering, but takes between two and three months to improve. In the poliomyelitis group I have yet to see a child develop hysterical paralysis through fear of the disease. But I have seen the opposite of this—a pathetic child of 10 pretending that its affected arm was strong, so as to avoid being sent to hospital away from home.

How can we recognise this functional weakness? First, the weakness is often associated with sensory loss affecting the whole limb Secondly, the examiner experiences, on gripping the affected hand, a feeling of power intermittently withheld and on gripping both hands together the normal hand will be weaker than when gripped alone Thirdly the wrong muscles can be felt to contract, and involuntary contraction is strong where voluntary contraction is weak. For example a man complains that he has no strength at all in his right leg if a hand is placed under the right heel while he is lying in bed and he raises his normal left leg against thigh pressure, a strong downward thrust of the right heel is felt There is also absence of muscle wasting while reflexes and electrical reactions are normal

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* An address given to the South Wales branch of the British [illegible] Association on April 3, 1954.

A nurse aged 23, had poliomyelitis affecting the left arm and leg In the second week of her illness when she was afebrile and doing well, paralysis of the right arm developed overnight and I was told that the condition had spread This was unusual in my experience and on examining the arm I found all the positive signs of hysterical weakness. I thought it important to get function back, and with a dose of thiopentone and suggestion her power returned I asked her afterwards why she had been so upset by her illness that she had believed her unaffected arm to be paralysed, and she told me that she was in a quandary She felt she should return home for the sake of her mother who had been left alone owing to a brother s call up but she was happy in her nursing and hated the idea of giving it up All was settled in the best possible tradition of British compromise by her taking a part-time nursing position near home

How should these hysterical palsies be treated? I think the doctor should explain to the patients that their memory for moving the limb has been lost because of some worry, trouble or anxiety, or because of the effects of the accompanying organic illness. After this suggestion under thiopentone is easy and usually successful, and the confidence thus engendered often helps these patients to confide their troubles freely

SENSORY DISTURBANCES

Functional symptoms occurring in physical disease may besides affecting motor function interfere with sensation. There may be either loss of sensation or increased sensibility to pain with a lowered pain threshold

Loss of sensation —Anæsthetic areas appear, usually peripherally or else down one side of the body, which do not correspond to the distribution of sensory nerves nor spinal-cord segments. The classical types are called glove and stocking in distribution The only organic diseases which produce a similar peripheral sensory loss are peripheral neuritis, where the tendon reflexes are sent and obliterative vascular disease where arterial ulsation is absent or diminished In the hemianæsthetic ses the loss of sensation is exactly midline; in the ganic diseases it does not reach the midline because overlapping supply from the normal side

I do not think any treatment is needed beyond pointing out that the symptom is of no importance and that it is not uncommon or unusual An assurance that the doctor has often seen this sort of thing before is useful

Pain —The most difficult functional symptom in organic disease is pain It can be a great trial and responsibility to everyone and I have made more mistakes over this symptom than all the others put together

I am sure that all pain should be regarded as organic until proved otherwise The commonest sites for functional pain are the head the back, the chest and the abdomen—in that order More and more organic abnormalities are being adduced to explain pains which [illegible]ty years ago I regarded as functional—fibrositis of the [illegible] temporal arteritis, spondylosis prolapsed intervertebral disc vasomotor instability—and I believe that some of these really exist and may produce pain

One or two clues are useful The pain, if not organic is described dramatically with a wealth of detail, and sometimes with bizarre distribution The pain is continuous "it never leaves me doctor," and (the most important simple diagnostic point of all) "nothing relieves it" This non response to good analgesic drugs is most helpful but not unfortunately completely reliable, because not only do neurotic symptoms occur in organic disease but organic disease occurs in neurotic people

I well remember a shockingly hypochondriacal aggressive difficult woman of 47 who plagued my outpatient department for three years with her complaints of headache like a heavy weight, doctor right in the middle here splitting my head open. She was admitted reasonably careful investigations revealed nothing and she was thankfully discharged Two weeks later she died suddenly while shopping and necropsy showed a tuberculoma of the falx between the two hemispheres. How right her description had been, and how wrong my assessment of her last illness.

Treatment of correctly diagnosed functional pain in organically ill patients must be sympathetic and unhurried We should explain that long-standing and relapsing illnesses may upset the nervous reactions of even the best intentioned patients We should not hesitate to assure them that they are having the best care and the best advice possible Only in this way will any benefit accrue to these difficult patients who are so exasperating and so time-consuming but often so frightened, so confused about themselves, and so unhappy Of one thing I am sure—so-called firmness of treatment can do nothing but harm The wisecracks and cynical remarks still made about these people reflect only on their makers who fail to realise how many symptoms are produced by doctors

CONCLUSION

In trying to show how some individual symptoms can be diagnosed as functional, and separated from accompanying organic disease I have emphasised some positive signs of this type of symptom rather than the absence of organic signs Suspicions will often be aroused by the general attitude of your patients I have found that the onset of a functional symptom commonly increases their demanding tendencies so that they lose the previous quiet acceptance of your skill and treatment that usually accompanies uncomplicated organic illness Do not blame them for this change—partly because you may be mistaken and then your blame will rebound on your own head but chiefly because your own annoyance, however justified, cannot help them and will cloud your judgment.

The great tragedy of course is to miss the organic. Therefore the physical examination of a patient ill for a long time must never become cursory and each examination should be as thorough as if it were the first Always remember that if you miss anything it is not because your intellect is failing but because you are not on the look-out for it.

NEW PROSPECTS IN RADIOTHERAPY

15 million volt Linear Accelerator at Barts

THE steady (and some may say sinister) advance in our knowledge of the properties of the universe went forward another step in a ceremony this week at St Bartholomew s Hospital in London On April 27 the Duke of Gloucester president of the hospital set in action a new 15 million volt linear accelerator which will in the next few years add considerably to our understanding of high-energy radiations and their effects on living tissue

To keep the hospital in the forefront of progress in radiotherapy (a position it has long held) the governors decided, in 1950 to install a machine that would help to expand the theory and practice of radiotherapy In the end the choice fell on the 15 million-volt linear accelerator—a machine which combines a high energy with a high intensity of radiation A contract was then placed with Philips Electrical for the machine to be built at the Mullard Research Laboratories Like its simpler forerunner, the X-ray tube, the linear accelerator is primarily a means of accelerating a stream of electrons The advantage of the new accelerator is not so much the high energy it imparts to the electrons but the great number of electrons it can handle Other types of accelerator, like the betatron or synchrotron, produce radiations of even higher energy, but their output is generally too low to make them a useful tool in routine radiotherapy

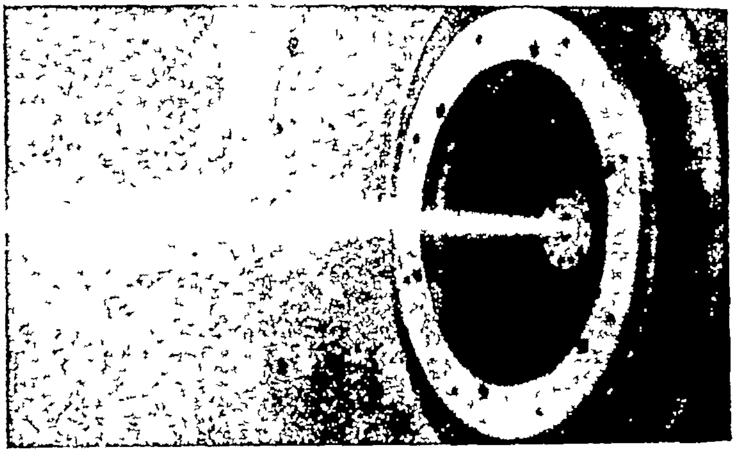
Fig 2—The electron beam leaving the accelerator

RESEARCH POSSIBILITIES

The treatment of malignant disease with X rays of high energy is, of course, one of the primary objectives, but the accelerator makes it possible to use either electrons or neutrons to irradiate a tumour Little is yet known of the effect of bombarding living tissue with these particles at high speed and in large quantities Much experimental work must therefore be done before the therapeutic possibilities can be assessed The neutron (being an uncharged particle) is difficult to keep track of, and uncertainties about dose-rates have hitherto deterred radiologists from attempting to extend the early work on neutron therapy The results of neutron therapy may be quite different from those produced by X rays, and this is perhaps the most interesting part of the new country that the accelerator will explore For one thing there is some evidence that it may be *possible to localise the action of the neutrons to* definite selected regions of the body As for electrons their range of penetration in tissue is limited (it is about 3 inches for 15 million-volt electrons), and under certain circumstances this property may be an advantage

But the new machine will perhaps be of even greater significance for the fundamental research that is planned into the biological action of radiations In many other ways the fearful prospects of the mismanagement of atomic energy are now all too clear, but we know very little about what an *ionising radiation* really does *in its* destructive course through a living cell If we did, it is just conceivable that we might be able to do something about it *The linear accelerator is particularly* suited to investigations of this kind, mainly because it emits its electrons in short bursts of enormous intensity, each lasting about a millionth of a second The dose rate during a pulse can reach something like 700,000,000,000 röntgen per minute All this means that the development of the changes in the cell can be followed with much greater precision than is possible with low-output machines and relatively long exposure times

For the next few years the accelerator at Barts will be devoted entirely to research on the biological action of radiations and on new techniques in radiotherapy During this time very few, if any, patients will be treated, so the machine has been installed in a temporary building in Charterhouse Square, next to the physics department of the medical college The work here will be directed by Prof Joseph Rotblat professor of physics in the University of London

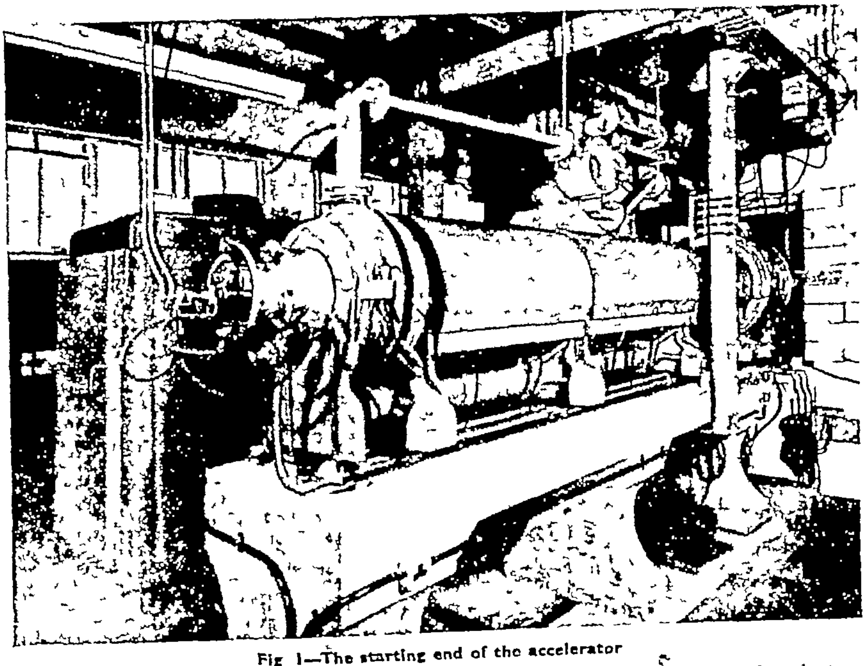
Fig 1—The starting end of the accelerator

The two vertical cables at the left hand of the machine run down to the electron in, behind which stands the cabinet housing the modulator The magnetron valve is en above the first section of the waveguide, and from it a system of pipes transmits [illegible] wave to the waveguide and back again The X ray head and the rest of the [illegible] e beyond the wall on the right

THE MACHINE

The principle of the accelerator is the use of a radio wave to pick up and accelerate electrons in an evacuated tube

An electron gun gives the electrons an initial velocity about two fifths that of light. This is achieved by applying a voltage of only 50 000 volts, which is the highest voltage used in running the accelerator. The electrons are speeded up by a radio wave travelling along a tube 20 feet long called a waveguide (its outer cover is seen in fig. 1). The velocity of the wave can be varied by diaphragms placed at intervals inside the waveguide. The wave can be made to pick up the electrons and deliver them at the other end of the tube with a velocity 90-95% that of light.

A valve called a magnetron supplies the waveguide with high frequency radio waves in short pulses. The power in the pulses is very high, about 2000 kilowatts, and about 40% of this can be delivered to the electron beam. The power from the A.C. mains is transformed by a modulator to produce high voltage pulses for the magnetron.

In the X ray head, where the electron beam emerges, there is a magnet which can bend the beam through 90°. The whole head can be rotated through an arc of 140° so that the radiations can emerge in any direction from 20° on one side of the downward vertical to 30° above the horizontal. The head contains a target holder which can be set in any of three positions: (1) no target (electron beam only), (2) platinum disc (X rays), and (3) uranium cylinder (fast neutrons).

The very high output of the machine raises difficulties in timing the exposure. To overcome this a special electronic device was designed and built in the physics department of St. Bartholomew's Hospital Medical College by means of which the exposure is terminated after any predetermined number of pulses from 1 to 10 000. In many radiobiological experiments exposures of a single pulse will be used.

The photograph we publish (fig. 2) illustrates more vividly than anything else the formidable power of the accelerator. The emerging electron beam is so intense that the area of ionisation stands out as a bright pencil of light, which rapidly fades away as the electrons are scattered by a relatively short passage through air.

RHEUMATIC UNIT AT EDINBURGH

A RHEUMATIC unit with 30 beds was started in the Northern General Hospital, Edinburgh, in 1947, and since 1948, when the hospital was taken over by the South Eastern Regional Hospital Board, it has been a regional centre for the diagnosis and treatment of chronic rheumatic disorders. At the instigation of Sir Stanley Davidson the University of Edinburgh created the whole time post of a senior lecturer in rheumatic diseases by whom the unit has been directed.

At first little in the way of research could be undertaken because both accommodation and staff were insufficient; but in 1949 support came from the Nuffield Foundation, which had just formed a clinical trials committee to administer a fund provided by Captain Oliver Bird, primarily for investigation into the prevention and cure of rheumatism and for relief of incurable cases. The Foundation made a grant permitting the employment of a clinical research fellow, a secretary, an almoner, and a clinical photographer, and the board of management found additional accommodation for the outpatient department and for research. With these facilities the unit has participated in the initial trials in this country of corticotrophin and cortisone and has made a detailed study of medical and social problems in rheumatoid arthritis. It has had continued financial help from the Nuffield Foundation and grants from the Medical Research Council, the Empire Rheumatism Council, and the Advisory Council of Medical Research (Scotland).

Last Saturday Commander T. D. Galbraith, Minister of State for Scottish Affairs, opened a new building adjoining the unit's wards.

It consists of two single storey blocks connected by a glass link which forms the entrance hall. One block is devoted to clinical work and laboratories, and the other houses the staff rooms, offices, and photographic suite. The plan is L-shaped and the main section contains six consulting rooms each equipped with examination couch, wash basin, built in blood pressure machines, and X ray viewing boxes. A waiting space open to the corridor is situated in the centre of the consulting area with dressing cubicles and toilets adjoining. Two laboratories and a conference room are at the end of this block, the laboratories having metal unit fitments which can be interchanged or added to later. There is also a small animal house.

The building is "contemporary" in design, but the construction is traditional. Internally the maximum use has been made of natural timbers, which are used to offset rich applied colour on various wall surfaces. A degree of informality is obtained by the extensive use of indoor plants and flowers. The furniture and fittings have been chosen by the architects, and are mainly of Scandinavian manufacture and design.

The total cost of this building, which was completed in ten months, was £27 000, inclusive of furniture and fittings. The Secretary of State for Scotland has leased the site to the Nuffield Foundation for five years, after which the site and the building will revert to the hospital as a gift from the Foundation. In addition the Foundation has promised £38 000 from the Oliver Bird Fund to meet the running costs during these five years.

Sir GEOFFREY GIBBS (chairman of the managing trustees of the Foundation) presided at the opening, and those present included Captain Bird. Besides Commander Galbraith the speakers were Sir HUMPHREY BROUN LINDSAY (chairman of the regional board) and Dr J. J. R. DUTHIE (director of the unit).

Medicine and the Law

Drug-addiction as "Cruelty"?

THE wife of a medical practitioner was given pethidine by a specialist at a time when pethidine was thought to be non habit forming, and became addicted to it. She importuned her husband for it by day and night, disturbing his work and his rest. He was advised not to give her that or any other drug involving injection, but he did not cease to do so. In May, 1952, the wife was certified and admitted to an institution, but in September she was discharged "relieved". She had no more drugs until in May, 1953, her husband gave her 'Omnopon' by injection to relieve pain from a sinus. She had to be certified again in July, but shortly after she was discharged 'recovered'. After that she worked as matron at a school and continued to behave normally without resort to any drug.

While she was under treatment her husband told her that he did not intend to live with her again, and in November, 1953, she filed a petition for restitution of conjugal rights. By his answer the husband pleaded just cause for refusing to live with her, and asked for a divorce on the grounds that she had become a drug addict and her resulting conduct towards him constituted cruelty. Mr Justice Wallington granted the wife the decree asked for and rejected the husband's prayer for divorce. The husband appealed.

In the Court of Appeal on April 20 Lord Justice Hodson said that the vital matter on the charge of cruelty arose in May, 1953, when the husband gave his wife omnopon knowing that it had a morphine basis and that his wife had been a drug addict, and having been warned against the very course he took. The conduct thereafter of which he complained seemed to follow from his act almost as night followed day. It was impossible to hold that conduct against the wife as cruelty by her.

Then it was claimed for the husband that although he had failed to establish cruelty the court ought, for a time at least, to withhold a decree for restitution of conjugal rights because in drug addiction cases there was undoubted danger of a relapse, and that risk existed here because the husband was a doctor and if his wife came to live with him again she would have access to drugs But the husband, in order successfully to resist a decree for restitution would have to show that it would be wrong to treat him as a deserting spouse (Russell *v* Russell [1895] pp 315, 334) The husband in this case could not show that The wife had shown herself willing to do what she could to rehabilitate the married life, and there was nothing to prevent an order being made in her favour The appeal should be dismissed

Lord Justice Parker gave a concurring judgment The Master of the Rolls (Sir Raymond Evershed) also agreed, but added that the husband's past acts in administering these drugs would not necessarily disqualify him from any relief in the future if the wife should come back and again succumb to any relapse and he should find he could not go on living with her The appeal was dismissed

Baby Dies after Fumigation of Pram

When an Oldham family moved into a corporation prefabricated house their hard furnishings, including the baby's perambulator, were fumigated with hydrogen cyanide[1] Later the baby became ill and died, and the parents and a daughter aged 2 had headaches and sickness Their pet budgerigar also died A forensic report said that traces of cyanide were found in the lungs and other organs of the baby and also in the dead bird At the inquest a pathologist said the presence of poison was a factor in causing the child's death He had also found evidence of dysentery In answer to a question, he said he did not know whether the child would have died of cyanide poisoning if she had not had dysentery death was due to a combination of the two The child's mother told how she had handed the perambulator, containing a mattress and clothing, to corporation employees She was not told to remove the mattress. In evidence an employee of the health department said that the family were told not to leave bedding in the perambulator Recording a verdict of accidental death, the deputy coroner found that there was no evidence of criminal neglect, but there may have been some "slip up" by a public-health employee

Hypersensitivity to Penicillin

A woman of 73 died within ten minutes of receiving an injection of penicillin[2] At the inquest her doctor said he had given the patient penicillin before without ill effects, but this time he noticed that she became flushed and breathless a few seconds after the injection. In spite of all he did she died within ten minutes A pathologist attributed death to the intravenous injection of a small amount of penicillin, to which the patient was allergic If she had not been abnormally sensitive she would not have died A verdict of "death by misadventure" was recorded

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[1] *Daily Telegraph*, April 22 1955

[2] *Evening Standard* April 22 1955

The Wider World

MEDICAL CARE IN A SOUTH AFRICAN TOWNSHIP

Mervyn Susser
M.B Rand

Zena Stein
M B Rand, M A (U C T)

Margaret Cormack
M B, Med B Sc Rand

Michael Hathorn
M B, B Sc Eng Rand

MEDICAL OFFICERS, ALEXANDRA HEALTH CENTRE AND UNIVERSITY CLINIC, JOHANNESBURG

Alexandra Township, with its 80,000 African and Coloured people living in an area of $1^{1}/_{2}$ sq miles, lies on the outskirts of Johannesburg It is one of the few places in the Union where Africans may own land The population is changing from a rural to an industrial society, the old extended family, which provided its own social security, is breaking up and slowly being replaced by the isolated, fragmented industrial family The men are employed in Johannesburg in the factories, in businesses, as domestic servants, at an average wage of about £3 a week Many women work in the city A growing number is employed in industry but the majority are washerwomen, nursemaids, and housemaids, sleeping in servants' quarters in Johannesburg and returning to their families on their days off A sprinkling of the population are shopkeepers and professionals

The Alexandra Health Committee has an annual budget of £70,000—less than £1 per head of population, compared with the budget of £28 per head in the adjacent Johannesburg area The Health Committee is expected to attend to the usual local government functions Being mainly a nominated body it has little standing wit [illegible] ple There are no sewers, sanitation and refuse disposal are inadequate, the roads are ditches (fig 1), and the streets are unlit Because of lack of funds no fundamental measures for the control of communicable disease can be undertaken

Budget studies by the staff of the Community Centre have shown that it is theoretically impossible for an Alexandra family to subsist on the average income Once rent, food, and transport have been allowed for there is no money left for clothing, blankets, or entertainment, nor is there anything with which to meet such disasters as illness, death, or unemployment

Most families rent one small room which must suffice for all their needs The staple cereal is maize, and white bread and oats are also used widely The main meal usually consists of porridge, a little meat, and perhaps potatoes Fresh fruit, vegetables, meat, fish, and eggs are in the shops, but are expensive and little used

With both parents at work and no after school activities girls and boys bring themselves up as best they can

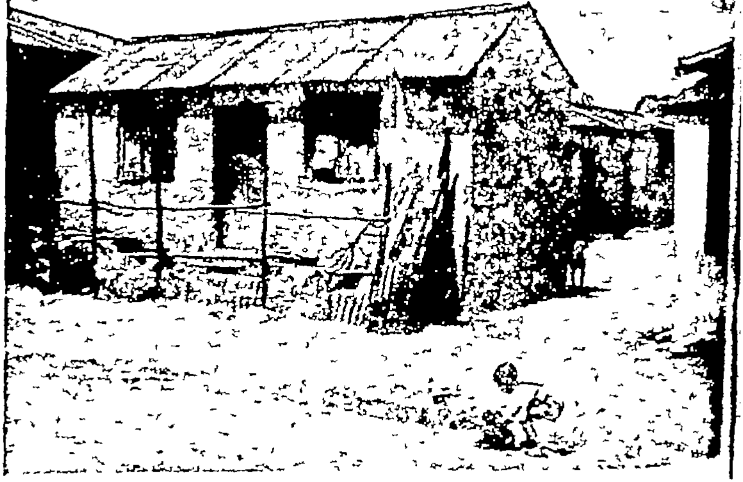

Fig 1—An average Alexandra plot seen from the street.

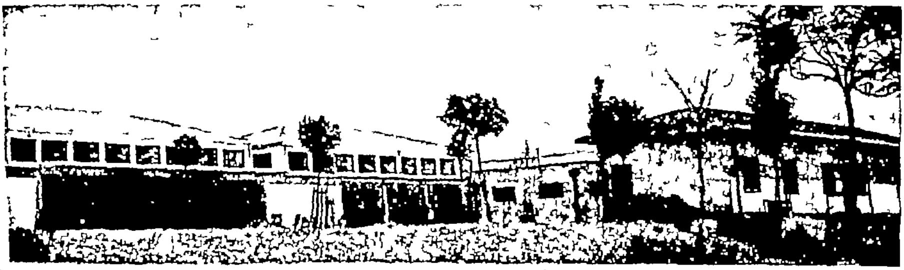

Fig. 2—The health centre and clinic.

Not infrequently the high-school girls have illegitimate babies or contract venereal disease while boys join gangs and embark early on a life of crime The police are ineffectual as protectors of life and property and at night the unlit streets have become notorious for bloodshed, rape, and robbery

Poverty and frustration and the unstable social conditions offer few incentives to sober citizens. Alcoholism is a tremendous problem, bound up with crime and venereal disease Fear of the white man his prisons and pass laws economic insecurity; fatigue from long hours of work and underfeeding—all give rise to emotional tensions.

The Health Centre

Among these 80 000 people the Alexandra Health Centre and University Clinic is the main medical service (fig 2) Administered by a board of management its funds are derived mainly from the university students rag, donations, annual contributions from the Transvaal Provincial Council and the Union government and patients fees In 1953 £20 000 was available and of this about £5000 came from patients fees Our staff consists of 4 doctors 4 sisters and 25 nurses who are helped by final year medical students who attend in groups throughout the year as part of their training

AT THE CLINIC

We hold consultations throughout the working day and we see urgent cases at any time For 1953 our statistics were:

New cases	12,500
Repeat visits	31 200
	43 700

wing to the perennial shortage of ospital beds we have to undertake more rocedures than the average outpatient linic. We have for example set aside a ecial room for patients, usually babies, ho need to be supervised over the day ere we are able to observe and instruct others in inserting eyedrops or in ving fluids to their dehydrated babies hile we record intake and output Sub taneous, and occasionally intravenous ansfusions are given where necessary e have found this arrangement invalu ble in training mothers and a help to us assessing the clinical status of patients

Within the last few years we have been ced with an ever increasing load of work he usual polyclinic system which peared to deal quickly with large umbers was tending to destroy the octor's relationship with his patient We e dealing with a people whose language istoms and economic pressures are very different from our own and they assume that we will treat them cursorily, as cases and not as people, unless we are able to show them otherwise We have found that the more prolonged and personal the relationship between patient, doctor and nurse the more we can achieve in both sickness and health

To maintain continuity between individual patients and doctors we divided the township into three areas A team consisting of a doctor a sister, nurses and students, is now responsible for all the curative casualty, and preventive work in each area Each doctor does the home visits for his own area and looks after his own tuberculous patients In this way we have gained continuity and efficiency and the patient has gained in personal contact Relations between doctor and nurse have also improved greatly as closer coöperation and understanding has become possible Team discussions in general health and nursing problems have proved valuable Our nurses are of the people speak the languages, and have much to teach us about the community On the other hand they are trained for hospital work only and there is much they have to learn about the concepts of disease health and health education We need regular and more frequent discussions but we do not easily find time for them We propose to introduce a family file system to give us a more complete picture of our regular families

The clinic is open night and day and the statistics show the heavy turnover but they do not show the amount of serious injury due to a disordered community

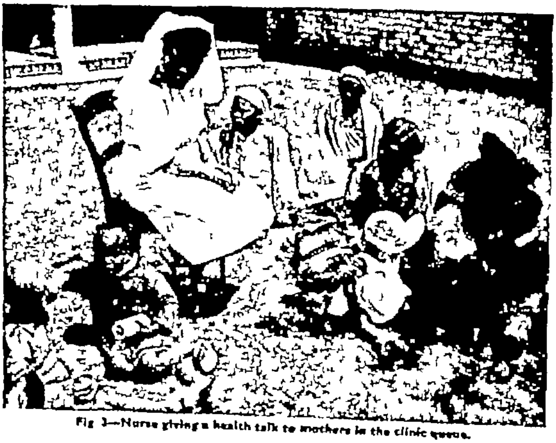

Fig 3—Nurse giving a health talk to mothers in the clinic queue.

life In 1953, first visits for dressings and injuries numbered 13,000 At weekends and on public holidays the casualty department is crowded We give emergency treatment such as intravenous transfusions for very shocked patients until we can transfer them to hospital

Curative work often drives out preventive work, and queues of patients forced us to neglect many of our intended health sessions Now we no longer give "health talks" only to the healthy and medicine to the sick We try to turn every contact with the patient into an opportunity for education We welcome re visits as a chance to consolidate our contact This attitude is difficult to maintain on crowded days, but the sick patient is peculiarly vulnerable to advice, and in so far as we have been able to carry out this policy, it has been a success

VISITS TO HOMES

Apart from midwifery calls, we made 16,500 visits to homes during 1953 Of these, the nurses made 13,500 calls, the doctors 2500, and students 1000

Nurses visit patients who have already been seen by doctors A patient with a high temperature and uncertain diagnosis whose progress needs daily reassessment, a patient with pneumonia who needs bed rest and daily penicillin, a cardiac patient who needs regular tests of digitalis and pulse checks, a patient in quarantine, demonstrations to a mother how to mix feeds or carry out treatment—this gives an idea of the range of cases on our district list Doctors and sisters take full reports from the district nurses each day and discuss their cases with them

Doctors and students do daily rounds Each firm visits weekly its own list of chronic patients, who are too ill and too disabled to come to the clinic These visits are a great comfort to the patients and give students some insight into the problems of the chronic sick

Even when the staff has been hard-pressed, we have kept up our home visits, for we are convinced that daily contact with patients in their own homes is necessary to our understanding of the people

TUBERCULOSIS

We are the tuberculosis officers for Alexandra, and this enables us to see tuberculosis as part of the general pattern of ill health

A man suffering from active pulmonary tuberculosis may be nursed at home or in "the settlement"—a cottage hospital for the tuberculotics in the township Here the patient is close to his family, in his usual environment, and the better in spirit for it The antibiotics usually render him sputum negative in six weeks, and we have found streptomycin, p aminosalicylate, and isoniazid effective even on ambulant patients at home Our patients have been cooperative and the defaulter-rate is low

In 1953, 548 new cases of tuberculosis were notified in the township Half of these were cases of primary tuberculosis, but case-finding and notification is irregular, and this figure gives no idea of the incidence of tuberculosis among children Of the adults, 80% could be classified as suffering from advanced disease at the time of notification Ignorance, superstition, fear of the disease, and fear of the stigma attached to it discourage a sufferer from seeking medical advice earlier

Thanks to government assistance, we are able to treat tuberculous patients and their families in a more integrated way than we do most of our other patients On receiving a notification, our health inspector visits the patient's home and brings back a report on the circumstances of the family It is his duty to explain to the family the disease and its implications and through h [illegible] to investigate all contacts

MATERNAL AND CHILD HEALTH SERVICE

During 1953 we delivered 2445 babies in Alexand Township, a large proportion of the infant populati All the mothers attended antenatal sessions, making average of 4 visits each Our nurses or students deliver the babies in their homes, and paid postnatal calls da for ten days The nurse explained the value of the po natal examination and the importance of the we baby sessions, and she advised each mother to attend t clinic in six weeks' time

Women pay a fee of £1, which entitles them to all t benefits of our maternity service We have tried emphasise to the mother the need for continuity maternal and child health by charging a compos fee to cover antenatal attendance, delivery, and medic care for the child up to one year of age

The midwifery service is long established and high thought of in the township, and we have had no difficul in persuading mothers to attend antenatal sessio For primitive conditions the corrected stillbirth rate (l in 1953) is good But we should like to offer mo health education at the antenatal clinics, which is t time when the mother should be taught how to look aft herself To hold our own against witchcraft and primitr beliefs, we have to teach some elementary concepts to o mothers Techniques must be explained in a way which simple yet fundamental To fill this need we ha instituted a system of antenatal home visits where t nurse goes over the talks given at the clinic We ha lately produced a simple film strip explaining the purpo of the antenatal clinic and its activities At the pos natal visit the nurse concerns herself mainly with t baby and with the establishment of breast-feedin

Successful health education requires long conta with the family, especially with the mother If she com to the postnatal clinic we know we have won her co fidence In 1953 about 66% of the mothers broug their new babies to the well baby clinic We try allow each new mother some minutes of individu discussion about herself and her family We outline t functions of the clinic, and explain the importance of t weekly dose of vitamin oil, of regular weighing immunisation, and correct feeding Each mother a baby is given a full physical examination Nurse th leads a group discussion on some of the questions th have been raised and tries to meet any difficulti (fig 3) Given time and staff, this postnatal visit c be the most important of all our contacts with patients In our experience it is a vital link in the mother's under standing of child care If the postnatal visits are hurr and neglected on a crowded clinic morning they lo most of their value

It is now left to the mother to attend the weekly ba clinic Statistics for 1953 show that 1429 mothers p first visits, and 10,941 repeat attendances were record

Our main aim in the clinic is to start the infant o sound diet We hope through the mother—the k person in the family—to change the dietary habits the whole family and eventually of the communit We teach mothers the nutritional values of differ foods, and we advise the use of cheap available fo stuffs for the infants rather than expensive brands baby foods We have tried to relate advice to act The Entokozweni Community Centre in Alexandra established vegetable clubs, a cooperative store, skimmed-milk centres When we discuss feeding proble we recommend the mothers to buy at these depots

Much of our infant mortality is due to preventa causes In the summer of 1953 nearly 100 babies d each month from summer diarrhœa Mortality in t disease is closely connected with malnutrition and wr feeding[1] Whooping cough also kills many babies He ducation must be our front line of attack on infant ortality, and the well baby clinics already play an ffective part.

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[1] Kahn, E M D thesis, Witwatersrand University, 19

Treatment in the Home

Poverty is inescapable in Alexandra. To improve ealth within the limits which it sets has been our main oncern.

Among the 16 000 families there were well over 00,000 calls on one or other medical service during 1953—i.e., more than one call per family per month. A reasonable charge for a private practitioner is 15s a call and 12s 6d a consultation. Few families can afford so much. In a slum population like this, the private practitioner cannot play an important role in illness neither can he strive for the frequent visits essential for health education. In Alexandra the clinic must act as the general practitioner. It must bring the family and home within its sphere and keep in close contact with the daily lives of the people.

In South Africa there is always a scarcity of accommodation in the Non European hospitals and the turnover of patients is rapid. The hospital doctor knows his patient only during the short crisis of illness he sees nothing of the events leading up to admission nor has he any control over convalescence and rehabilitation. Through our domiciliary practice we have come to understand something of our patients' background.

In hospital, the African is too often the passive recipient of injections and medicines. He learns nothing in this foreign environment of the nature of his illness, its cause and its remedy. The hospital rarely helps him to understand his disease nor equips him to deal with it.

We were first driven to nursing seriously ill patients in their homes by the difficulty we found in arranging hospital beds. Our confidence in home nursing has grown as we have realised its possibilities. To the African patient hospital is a strange world of white sheets and strange white faces. He has a strong belief that people go to hospital to die. For children particularly to leave home is a traumatic experience. We find that the care of the unskilled but carefully instructed mother will often do more for the patient than less concentrated nursing in an understaffed pædiatric ward. Cardiac patients, who used to be always in and out of hospital are now ambulant and well-controlled they have come to understand the principles of maintenance therapy and the importance of regular visits. Relapses are usually managed at home and the patients seem to be happier. The results of treating tuberculosis in the home are encouraging we have no doubt that ulter rates are reduced and that patients are more ly to undergo prolonged treatment at home than hospital. In midwifery we have found the African ther to be relaxed and coöperative and a very cient parturient at home. A good local hospital ich deals with a comparable group of mothers does better our results. When we deliver a baby at home, preserve the continuity between antenatal and postal care. The confinement is brought into proper spective as part of a process that began with con tion and will end when the infant has attained healthy ldhood. In this community which is unfamiliar h scientific medicine, domiciliary practice has much offer that the hospital does not give.

Our nursing staff is learning to contribute more to the ication of our patients. With further training in the nic and more time to spend with each family nurses can much to combat ignorance and prevent disease. rough their domiciliary visits medical students learn appreciate the potentialities of practice outside the spitals and see how environment affects disease.

We have tried to learn something about the people d with this knowledge to adapt our service to their eds. Some useful principles have emerged and the nic has improved the health of many people in Alexandra Township, but it alone cannot make Alexandra a healthy town.

We wish to thank Dr S L Kark for the stimulus of his ideas and advice Dr Cicely Williams for her encouragement and assistance and Miss Helen Navid of Entokozweni for the guidance she has given us in sociological matters. We are indebted to Dr A. D Bensusan for the photographs and to the Board of Management of the Alexandra Health Centre and University Clinic for permission to publish this report.

Parliament

Poliomyelitis Vaccine

IN the House of Commons on April 25 Mr IAIN MACLEOD Minister of Health made the following statement on the Salk poliomyelitis vaccine.

I know the whole House will wish to congratulate Dr Salk on what is clearly a momentous and historic advance in the protection of human well being. The Health Departments and the Medical Research Council have been in close touch with these developments in the United States.

For our part we shall go ahead with the increased production of the new vaccine. In this country two important firms are already arranging to do this as fast as possible and it is the Government's intention to ask these firms to sell to the Government their whole output. In due course a supplementary estimate will have to be submitted to the House for that purpose. No supplies, in any material quantity are at present obtainable from the United States. Home production should assume really useful dimensions by the late autumn and I am advised that it would be medically unwise—even if it were possible—to embark on any large-scale vaccination during the peak season of the disease which begins to end about then. It is, for example quite usual for diphtheria immunisations to be suspended during the prevalence of poliomyelitis.

Many interpretations have been put on the attitude of this country to this development. Perhaps it is as well to put the facts in plain words to the House. This new vaccine involves inoculating our children at repeated intervals with a preparation derived from the kidneys of dead monkeys. The House and the country will surely agree that we must carry out intensive tests as to the exact effects so that we can eliminate any possible dangers from it. We are already doing this. We must also make sure as we shall, that it is effective against the particular strains of the virus most commonly found in this country. indeed it is not sure yet that it is fully effective for children of about four or under where our incidence of the disease is highest and it seems it may be less than normally effective against type I of the virus—the commonest type over here.

I mention these reservations because it is important to keep the picture in true perspective. But they in no way detract from the immense humanitarian value of this great discovery or affect our determination that our own people should benefit from it to the fullest possible extent.

Mr N N DODDS: Is the Minister aware that this year the Americans are treating $13^1/_2$ million children? Would he agree that they have made excellent tests? Despite all his reservations can we have an assurance particularly as this vaccine was produced in Canada that we are not making excuses for the very slow way in which we have taken up this vaccine?—Mr MACLEOD I do not see how anyone can make a charge like that. This report came to us by air last Tuesday. A great deal of intensive work has been going on since then and in my statement I have given an undertaking that we will buy the output of the firms in this country who are making the vaccine. We will go straight ahead so that our people can benefit from the discovery as soon as possible. However I am sure it is right to mention to the House the reservations one must have on such an important matter.

Mr WALTER ELLIOT I am sure that the whole House will support the Minister in his desire to have these matters tested before embarking on any large scale treatment of the children of this country but will he publicise the lines of the tests which he is considering? If he could give some information about his investigations I am sure it would do much to reassure opinion in this country.—Mr MACLEOD: The question of research is essentially one for the Lord President of the Council but I understand that the Medical Research Council is carrying out trials in Southend Manchester Sheffield Belfast and I think Glasgow.

Mr H A **MARQUAND** Does what the Minister has said mean that he expects that by the late autumn the tests will have reached such a stage that it may be possible to begin inoculation ?—Mr **MACLEOD** Pilot batches of this vaccine are already available for testing One would hope that all the necessary testing will have been finished by the autumn and that substantial quantities of the vaccine—it is difficult to estimate how much, but between 500 and 1000 litres—will be available to us by the end of the year

Replying to a further question, Mr **MACLEOD** said that the *major limiting factor* at the moment, and for some time to come unless a new medium of cultivation were discovered, might be the shortage of monkeys The Government had already taken action to contact the government of India on the matter and the Medical Research Council had already sent representatives to Africa to study the possibility of further supplies of monkeys from there

Social Services and the Budget

In his Budget speech in the House of Commons on April 19, Mr R A. **BUTLER**, the Chancellor of the Exchequer, said that the bread subsidy cost £41 million, and the welfare subsidies, including children's milk and so forth, at least £36 million At the beginning of 1954–55, apart from the Exchequer contributions to the National Insurance Funds, the social services were expected to cost £1260 million They had, in fact, cost £1278 million, and for 1955–56 it was expected that they would cost £1315 million Comparing the original Budget estimate for last year with the estimates for 1955–56, the health service showed *an increase of* £32 million, education, including grants to universities, an increase of £25 million, and war pensions, following the recent rise in the rates, an increase of £8 million The Exchequer contributions to the National Insurance Funds were also *a growing and inescapable commitment*, and in the coming year they would demand £100 million, compared with £78 million for last year The increased cost of these items amounted to £87 million, which was more than the whole of this year's increase in Civil Supply This, *Mr Butler said*, was striking evidence that in this field of social services a growing burden on the Exchequer was to be reckoned with Much of the increase in expenditure was *contractual*, while the remainder represented what he was convinced was a worth-while investment in the future well-being of the country Investment in human health, wider opportunity, and increased technical skill, meant something *more than* "*investing in success*" *It meant* the assurance of a happily working and socially responsible democracy But if we were to carry this burden we must not only maintain the increase in the national income but also be constantly watchful that all our existing services are administered *as economically* as possible We must examine with a critical eye all the many additional claims which were constantly being made on the Exchequer for new services, so that the basic social needs of our people came first

Mr J A **SPARKS** asked why, *if the Chancellor had* money to spare, he had not used some of it to improve the National Health Service ? For example, why not *reduce the* dental and optical charges and the prescription charge, and waive the charge for appliances for disabled people altogether *Last year the Government contributed* £9 9 million towards child care, and in 1955–56 they proposed to contribute £9 7 million, a reduction of £200,000 But during the last two or three years the policy had been to reduce the number of day-nurseries throughout the country, squeezing out these children and depriving industry of the labour of able and capable young women, just because they had children Another direction in which the Chancellor might have used some of his surplus was in reducing the interest rate for housing loans or in providing interest-free loans for that purpose

Foot-and-mouth Disease

In the House of Lords on April 20, the **EARL OF LISTOWEL** drew *attention* to the Gowers report which had unanimously stated that in dealing with this disease vaccination was no *alternative* to one *traditional* policy of slaughtering infected animals and contacts He asked the Government accepted the Committee's ations, and in particular what were the Government's views on the use of vaccine during an epidemic, and on the proposal to set up a veterinary research council

In a *maiden speech*, *Lord* **ADRIAN** said that the Gowers Committee, of which he was a member, would have been glad to recommend a different method of controlling this disease, but they were forced to conclude that the slaughter policy for the present was cheaper and safer *than any other* Vaccination had been tried on a large scale and, within limits, had been extremely successful In countries where the disease was endemic the slaughter policy was impossible, *and* there the only possible method of coping with it was by vaccination But vaccination still had considerable limitations No-one claimed that vaccines gave 100 % protection Young animals could not be immunised at all, and in adults the *dose had to be* repeated every six months There was the usual difficulty with virus diseases, that an unexpected strain might turn up which rendered the vaccine prepared from the usual strain ineffective

Britain was fortunate in belonging to the group of countries which had natural barriers against infection Foot-and-mouth disease had never become established in Australia, New Zealand, Canada, the United States, or here We got only occasional infection from the Continent which could be dealt with by the policy of stamping out which was far safer than wholesale vaccination would be But vaccination did raise the resistance to infection and the possibility had been investigated of *using it as an additional safeguard* Some *countries* which, like us, slaughtered infected animals and the contacts, also built a ring of immune cattle around the outside of the infected area But the committee could find no clear evidence that this policy would be effective in the conditions that existed in this country The committee were attracted to the idea that valuable herds of cattle might be preserved by vaccination when an epidemic threatened *from* abroad, but decided that even that limited use of vaccine would be too risky to allow at present If it was certain that vaccination would give 100 % immunity, it would be reasonable to allow prize herds to be protected in this way, but with only 90% *immunity there would be a risk of masked* infection

Vaccination might never be the right method for this country On the other hand, we were threatened every few years by the big epidemics on the Continent, so any improvement in vaccines would be to our advantage *Though we did not use vaccines ourselves*, it was m important that the Government research station Pirbright should go on experimenting with th Pirbright was not only our research centre, it was al an insurance against possible disaster It was con*ceivable that* we might be faced with an epidemic fr the Continent too severe to be controlled by slaugh In such an emergency the Continental countries w themselves need all the vaccines they could manuf and we should have to rely on what we could make h Pirbright would *have to make it* or to supervise production Lord **ADRIAN** knew that steps had be taken to enlarge Pirbright and he hoped that it w be enlarged sufficiently At the moment there was a l in the foot-and-mouth front, we should use it to our defences

EARL ST ALDWYN, joint parliamentary secretary the Ministry of Agriculture, said that the Go accepted the Gowers Committee's recommendation the stamping out policy was right for this country normal *times*, but that vaccination might be valua in an epidemic so serious that slaughter was n practicable nor economic, but the Government took view that an outbreak would have to be except bad—much worse than anything so far—before the of vaccination would be *justified* It would have to left to the Minister to decide whether, and, if so, whe impose vaccination Frankly, the contingency se rather remote He admitted that experts disagreed the possibility that vaccination might mask inf but until we knew for certain that no such danger ex the Government believed that the risks to the far community as a whole would outweigh the benefit individual farmer might gain from vaccination of particular herd

The further expansion of Pirbright Institute wa matter in which the Government felt they ought oceed carefully It might be that no more physical pansion would be needed, provided there was a reserve pacity of output that could be called into use if cessary The Gowers Committee had suggested that might be worth while considering whether a separate eterinary Research Council ought to be created That estion had been raised some time ago with the Privy uncil but it was felt that it would be a retrograde step separate research in animal crop and soil husbandry l of which are the responsibility of the Agricultural esearch Council

The Government also accepted the recommendation hat private collectors of waste food for animals should e licensed and the swill sterilised They were not, owever prepared to extend this requirement to swill ollected by local authorities, since they feared that it ould deter local authorities from collecting kitchen aste separately Kitchen waste would then be dumped ith other refuse where it was impossible to prevent all isk to animals

QUESTION TIME

Dentists' Remuneration

Replying to a question Mr IAIN MACLEOD Minister of Health, said that after a full investigation into earnings and practice expenses the Secretary of State for Scotland and he had agreed with the British Dental Association on an ncrease in the present remuneration of general dental practitioners.[1] A new scale of fees was being worked out and the ecessary regulations would be laid before the House of ommons in due course The new scale would be designed o give dentists a net income comparable having regard to he volume of work done with what they would have received n the period covered by the investigation had the 10% duction not then been in force They had also agreed as an terim measure while the new scale was being worked out o cancel the 10% reduction in the present scale Regulations ith this effect would be laid as soon as possible They timated that the cost of these changes would be about 1 million in a full year

Increased Expenditure on Food

Replying to a question Sir EDWARD BOYLE, economic retary to the Treasury said that of the increase of 16% consumers expenditure on food between 1952 and 1954 arly half—representing a rise of 7%—was an increase in lume and the rest a rise in prices The standard of living the average weekly wage-earner which fell considerably ween 1947 and 1951 had risen considerably since the ter date.

Financial Loss on the Remploy Scheme

Replying to a question Sir WALTER MONCKTON Minister Labour said that the excess of expenditure over income Remploy Limited was estimated for the period ended rch 1 1955 to be £2 430 000

School children and Milk Tablets

Replying to a question Mr D F VOSPER parliamentary retary to the Ministry of Education said that milk tablets re being used in about 800 schools in England and Wales. e Minister approved their use only where the education thority was unable to make satisfactory arrangements for upply of fresh milk. He hoped that fresh milk would rtly be available again in practically all cases. It was the nister s desire that liquid milk at a reasonable price should supplied to all schools and he had no doubt that this estion would come to the notice of the people in the areas cerned The number of schools to which milk could not be pplied on account of their inaccessibility had shown a nsiderable reduction over the last three years and it was ped that that would continue

Mr HASTINGS: Does the Minister realise that milk tablets never take the place of fresh or pasteurised milk and that the preparation of tablets important substances are moved which are not replaced unless special conditions ply? Mr VOSPER: Yes. Milk tablets are really a substi e for reconstituted dried milk to which I think they vide a more palatable alternative but they are no sub tute for liquid milk. The large number of cases have arisen through inaccessibility but because of a dispute which ope is of a temporary nature

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[1] See *Lancet* April 23 1955 i 874

In England Now

A Running Commentary by Peripatetic Correspondents

HOPES of a cure for arteriosclerosis have been revived by exciting news from China. Scientists have long been puzzled by the apparent immunity of the Chinese to arteriosclerosis. Therefore, the discovery of a new drug, prepared from the muck weed *Yen Wu Pong* and given the approved name of hydroxypropyl *nor* yen wupongine, is not without interest

The credit for the first thorough investigation must go to workers at Barthomary's Hospital where 7 patients with thickening of the radial arteries were given H N Y W P by continuous intragastric drip for 47 hours. Careful palpation of both radial arteries only three months later showed complete arrest of the disease process in no less than 71% of cases. One patient died of coincidental lymphosarcoma and one took his own discharge In the light of these findings further investigation was deemed reasonable

A large-scale clinical trial was then instituted by the Arteriosclerosis Research Panel, urgently formed by fellows of the Royal Colleges with a personal interest in the problem The panel was commendably cautious in its interpretation of the Barthomary series, since no controls were used and wisely insisted that the trial should include at least 5000 treated and untreated cases. Also, in view of the need for certain special clinical and pathological observations—e.g pulse and sedimentation rate—supplies of H.N Y W.P were restricted to the teaching hospitals. A shortage of clinical material proved an early obstacle and it was found necessary to appeal for suitable cases of essential hypertension, coronary sclerosis cerebral thrombosis, gangrene and senile dementia It is only fitting to record the magnificent and magnanimous response by most non teaching hospitals

Some important facts were brought to light. For instance it was conclusively established that where both cerebral hemispheres had softened as the result of hæmorrhage, the lesion was irreversible and the administration of H N Y W.P could serve no useful purpose No definite conclusions could be reached as to the earlier claims from China and Barthomary's, but it was recommended that provincial hospitals undertake further trials The panel added the interesting observation that a statistically significant number of chronic bronchitics were afforded symptomatic relief during the trial

* * *

The departure of our living in maid for a post in which she is to be paid what is almost my salary before deduction of tax has led me to consider with scientific detachment the problems of running a house I have been appalled by the time which women waste in their homes. The basic fault is psychological and only a change in mental attitude a sort of rearrangement of conditioned responses, is needed to give them a great deal of leisure

After only a few moments concentration I devised for example a rapid method of making beds. Instead of tucking in each sheet and blanket separately all the bed-clothes were straightened en masse by rapid tugs at their lateral edges; even the process of airing was eliminated and no cold damp air substituted for the warmth of the recently occupied bed. My wife received this time-saving manœuvre with the horror of one who is incapable of reasoning from first principles even though my results were shown to be identical with hers.

A further proof of the power of habit and propaganda over intellect is the reverence with which women regard absolute whiteness If advertisements would extol light grey as an ideal of excellence we should save much time particularly in the family wash.

Again, take dust Women regard a light film of dust on furniture as a blemish and spend valuable time in removing it Yet they actually put dust on their own noses. While I should be against an entire reversal of attitude towards noses and furniture I think that a little conditioning would induce women to regard a matt surface on furniture as desirable as a bloom on a peach

Washing up is another branch of household management which needs scrutiny by men. Cups, for example are by custom washed all over whereas only a small section of the and the bottom actually require this attention. Plates which may merely need a dusting are always placed in the washing-up bowl. Incidentally one plate can nearly always be made to do the work of two. Stainless steel sheeting on table tops would at once abolish table cloths and the need for washing them.

By suitable suggestion and propaganda, I believe one might even modify that astonishing feminine reflex, loosely termed "spring cleaning" as though it happened at only one season in the year. My own slogan, NO DIRT—NO COMFORT, has so far yielded little result but one has only to think of that cleanest of all rooms, the operating-theatre, to envisage the antithesis of cosiness. Who could imagine an operating-theatre containing a really comfortable arm-chair, a man smoking a pipe, an open coal fire, and a sleeping dog? Surely it is not beyond the wit of men to fashion a domestic world in which it would be comfortable and restful to live—in fact a world that was not too clean.

* * *

When the tobacco-smoke has cleared a little, could somebody please give thought to the automobile as a biological hazard. I don't mean road-safety, or exhaust fumes. Nothing mechanistic like that. If the anthropo-automobile relationship were given as much attention as, say, fluoridation of public water-supplies we might elucidate coronary thrombosis perhaps, or peptic ulcer. Driving a car does something to the driver as well as to the car. Women have their style of driving. So have teen-agers. Different cars respond differently. Every car has a personality—its *innate characteristics modified* by its environment—which reacts with the personality of the driver. Put a lorry-driver behind the wheel of an MG—would he melt into the mechanism like an undergraduate? There is a biological synthesis in car-driving which we as a profession have ignored. The manufacturers have glimpsed it. "Sparkling performance," they say, implying an individual response to a stimulus. But you've heard the grunts and growls from some of these cars. And what is happening meantime to the owner's systolic pressure or gastric acidity? Couldn't we add to our clinical histories a few notes on the patient's motoring record? Type of car driven, how long, performance, pathology, &c. Just think of the people you know and what happens to them on the road—you'll begin to see meaning in the cold starter, the trouble with the clutch, the heavy consumption of oil. I've talked to the folk at my garage about this. They don't see it. What do they know of engines who only engines know? Besides, the idea really had to strike you before you get it. My car went on fire that summer before the introduction of the N H S. No organic cause was found.

* * *

Our physician has always described the thinning seen in the X rays of some skulls with chronically raised intracranial pressure as "pewtering." He accordingly sent a request to the X-ray department in his usual shaky handwriting: "Skull ?pewtering." But our new radiologist has always used the term "beaten silver." So his report unexpectedly ran—"Two earrings are seen but no pewter ring."

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SONNET TO NEGLECTED ORGANS

"Poets have rarely written about the pancreas, lungs or thyroid gland."—I. Davidsohn, M.D., in the *American Journal of Clinical Pathology*, March, 1954.

O Pancreas! I know not what thou art,
Thy islets formed of several kinds of cells
Producing insulin, and something else
Whose name I have forgotten, fill my heart
With wonder, while the lungs to me impart
Their secret motions when the bosom swells,
As seen in those assailed by noisome smells
Or stricken with the wound of Cupid's dart.

But ah, for loveliness that cannot fade
Give me the thyroid, shall I call thee gland?
Within thy vesicles the hormone made
Governs the bulging neck, the trembling hand,
Thou makest lids to lag, and eyes to stare,
patients to discard their underwear.

Letters to the Editor

GENETIC EFFECTS OF THERMONUCLEAR EXPLOSIONS

SIR,—Dr Bourdillon (April 23) is right in thinking that some human mutations could be beneficial but many associated questions come immediately to mind. Are we sure that at its first appearance we would recognise an ultimately beneficial mutation? Are we making full use of those that already occur? Are we satisfied that to get any necessary mutations, it is better to clutter the atmosphere as a whole with radioactivity rather than to expose selected gonads to it? And, finally, have we a satisfactory policy for coping with the defective and monstrous mutations which everyone agrees will greatly outnumber the beneficial ones?

The effects of a given mutation rate clearly depend on the intensity of genetic selection. Under very primitive conditions, with heavy selection, mutation may be advantageous in producing a variety well adapted for life in that particular environment. But, as we get more civilised, the development of sympathy, coöperation, and the medical services goes a long way towards abolishing the selection that originally produced Man. Without selection, mutations are a menace and it is an illusion to think that there is any harmless level of radiation. The random operation of cosmic rays, potassium, radioactive rocks, and other mutagenic agents may well have mediated our early development, but we now exist in spite of them and not because of them. There is little we can do to keep off these agents and ultimately it may be necessary to replace the accidents of natural selection by the methods of the stockbreeder so as to get rid of the accumulated harmful mutants. That is a problem that we can tackle when we are a little clearer about the qualities with which we would endow the ideal human being. Meanwhile, it is surely wise to avoid any conditions that may increase the load of mutations.

Harpenden, Herts. N. W. PIRIE.

PSORIASIS SPONDYLITICA

SIR,—The term "psoriasis spondylitica," used by Dr Fletcher and Dr Rose (April 2) to describe cases in which psoriasis and ankylosing spondylitis co-exist, cannot, in my view, serve any useful purpose, and it appears that the authors themselves were dubious since they quote William of Occam at the head of their paper. To draw attention, however, to this clinical association is of the greatest importance, as I hope to indicate in this short letter. Owing to ever-increasing specialism, syndromes arising from a common pathological stem, now emphasising one and now another feature, according to the specialty of the observer, lead to a multiplicity of descriptive terms which, by their very multiplicity, obscure their *common origin*.

In the field of rheumatoid disease, we know that rheumatoid arthritis, iritis, and psoriasis may occur singly or severally combined. That sex, genetic influences, &c., may modify the point of attack in the tissues should not, however, divert our minds from the essential unity and basic pathological features of all these syndromes and so lead to numerous descriptive terms. It should rather stimulate us to seek an explanation of the differences against a background of a unitary concept.

It is with confidence, therefore, that I now discuss Reiter's syndrome in an attempt to further this unitary approach. Here we find again that rheumatoid arthritis, spondylitis, iritis, and keratodermia blenorrhagica (which is indistinguishable from psoriasis) may all again be severally or singly associated with urethritis in the male. The urethritis, it must be stated, may be as florid as gonorrhœa or may merely consist of threads in the voided urine, with all gradations in between these two extremes.

Knowledge of Reiter's syndrome has, since the war, ablished certain clinical facts which may not however, generally known

(1) It has been clearly established that the systemic com rations of arthritis (rheumatoid type) iritis and kerato rmia blenorrhagica so long attributed to gonorrhoeal infection ve nothing whatever to do with this disease and such ms as gonorrhoeal rheumatism &c should be deleted om the literature Present clinical knowledge shows that ese complications arise from non specific urethritis, and at when they follow a known gonorrhoeal infection a dual fection is present from the outset

(2) Reiter's syndrome may exist either as the complete icture described by Reiter or as formes frustes, where nly some of the features appear Cases are known to occur ither after (*a*) bowel disorders—i.e various dysenteries— r (*b*) sexual exposure

(3) There is no comparable disease in the female associated ith urethritis.

I contend that these facts must be woven into our nowledge of the rheumatoid diseases if we are to get ny clear picture of the various syndromes I would like o mention some other significant facts which go a long ay to explain why tissues so apparently different s joints, eyes and skin should be the seat of attack:

(1) Of all bodily tissues, the joints, skin and eyes contain e highest proportion of hyaluronic acid the substrate hyaluronidase

(2) In the body hyaluronidase is only found under normal nditions in the testes.

(3) Hyaluronidase is secreted by many organisms, especially e streptococcus, which has been traditionally associated ith rheumatoid disease.

(4) The rôle of hyaluronidase is that it facilitates penetra n by an organism of the very tissues affected in rheumatoid ease and the clue to the discovery of the specific organism is in the now well known disease termed non specific rthritis.

Finally reverting to the article by Dr Fletcher and Rose one would expect that case 3 and probably e 2, should show signs of urethral abnormality, at least the presence of threads in the two glass test for the ure of the disease is that which has so often been n in Reiter's syndrome As I have long held that riasis is a manifestation of the rheumatoid group ope that dermatologists will heed the valuable advice en by Dr Fletcher and Dr Rose and search amongst ir abundant material for further cases of this nature.

London W 1

F L LYDON

ROPHYLACTIC PSYCHIATRY IN CHILDREN'S HOMES

SIR,—The article by Dr Neustatter in your issue of ril 16 is very welcome It is most reasonable to expect at these young psychotic casualties will develop more rmal personalities with such prophylactic measures n they could have done if left in the environment ich gave rise to their difficulties.

In the field of mental deficiency rich rewards await ventive psychiatric treatment I refer to the inaugura n of babies hospitals apart from colonies of adults ldren's and babies hospitals are just as essential for treatment of mentally ill children as they are for treatment of other diseases—and doubly so when child is born with its illness as in mental deficiency bies hospitals could accommodate children from ancy up to five years old

rom intensive therapy in such units for the mentally fective one would expect the following benefits

(1) *Habit training* This, done by experts in the ideal milieu the proper habit training time should lessen the big nursing blem attached to the low grade adult population in the sent-day hospital for the mentally defective

2) *Speech training* Intensive work by the expert speech rapist at the normal speech learning period should cut out much of the inarticulate speech which is such an added handicap to many mental defectives.

(3) *Orthopædic treatment and physiotherapy* could be instituted earlier with better final results; and much spasticity associated with mental deficiency could be relieved by suitable training of the very young child.

(4) *Special training* Observation and assessment by the psychiatric personnel would be able to decide which children could benefit by education in the 3 Rs and which in practical skills, and thus save much time and money in educating unsuitable types.

It may be that such hospitals exist in full therapeutic and research usefulness I understand that there are babies' units attached to large colonies for mental defectives, but I have not read results therefrom Certainly in this area our mentally defective infants material remains in the lap of the mothers one of whom recently told me that she carried her problem from doctor to child welfare centre to hospital to specialist to mental deficiency officer, but always back home again It is probably a matter of money but intensive therapy in a hospital for mentally defective infants might save much by preventing a long stay in hospital later and by making useful material out of what must, under present circumstances be permanently useless

Morpeth, Northumberland

J H. THOMPSON

RUPTURE OF LAPAROTOMY WOUNDS

SIR,—As the pioneer of the use of nylon for suturing the abdominal wall[1] I am very interested to find that others are using it with satisfaction From my own experience of many hundreds of cases sutured with nylon or catgut I have formed fairly definite opinions of the advantages and drawbacks of the former

(1) The use of the thicker sizes (no 5 upwards) increases greatly the risk of discomfort and chronic sinuses in the wound I have used mainly no. 3 myself and the incidence of sinus formation has been very low even in infected cases. At the same time I have removed quantities of the thicker sizes inserted by others. Tissue reaction is known to be greater with multifilament than with monofilament nylon and it would seem that it may be related to the surface area of the material used

(2) The tensile strength of nylon, as served up in the theatre, varies considerably in spite of the maker's claims of uniformity even though it has been sterilised on the one occasion only My theatre staff are also definitely of this opinion We have tried various methods of sterilisation without any noticeable difference I must agree with Dr Greenwood (April 9) that nylon can at times snap with disconcerting ease and it should be well tested immediately before use This criticism applies to multifilament as well as to monofilament nylon.

(3) The monofilament variety is the one which has the advantage over other non-absorbable suture materials of being solid, but it has the drawback that it breaks easily at knots or when sharply angled

Experimental work has indicated that wound healing is quicker and safer with non absorbable sutures than with catgut and my clinical experience supports this conclusion. However the lack of tensile strength in the finer varieties of nylon and the tendency to sinus formation and wound discomfort when thicker varieties are left in situ, have led me to develop a technique whereby the buried sutures can be removed after the tissues are soundly healed. A continuous interlocking chain stitch with no 8 nylon identical with that made by children's sewing machines is inserted with a Reverdin type needle both ends and the terminal loop being brought through the skin The loop is held over a piece of rubber tubing and Finesay buttons are applied to the two free ends After two weeks or more, when the wound is considered strong the rubber tube is slipped out of the loop and the starting end of the suture is cut short after which traction on the other end withdraws the whole suture

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[1] Haxton H *Brit med J* 1945, i, 12

This method has the advantages of the good support and quick healing associated with non-absorbable sutures, combined with freedom from the spectre of chronic sinus formation The method has been in use for 18 months, in parallel with a series in which 40 day catgut was used, and it works well It has the advantages over through-and-through or figure of eight sutures involving the skin of being much less painful and leaving less ugly scars

I should like to add one comment on the technique, described by Mr Oldham (April 16), of using a doubled suture, cutting the terminal loop, and tying the ends together In this method the terminal loop is of single strand thickness, and a suture, like a chain, has the strength only of its weakest part I agree with him that it is easy, and desirable, when burying suture material to tie the initial and final knots on the peritoneal aspect of the aponeurosis

Manchester HERBERT HAXTON

CARBONIC ANHYDRASE INHIBITION

SIR,—As acetazoleamide ('Diamox') can lower the arterial-blood CO_2 level it would seem to be the ideal diuretic to use in the treatment of emphysema heart failure because respiratory acidosis is common in this condition In your leading article of April 2 you mention the favourable results that have been reported[1 2] in the treatment of emphysema heart failure and respiratory acidosis respectively My experience, though limited, differs from that of the workers you mention

There is no doubt that diamox can cause a diuresis in heart failure of varying cause, but in assessing its value in emphysema heart-failure one must remember that an acute respiratory infection may precipitate cardiac failure in an emphysematous patient and that the œdema clears as the infection subsides Diamox should therefore be tested in those with chronic failure and a "stable" chest Such cases are uncommon I have treated 2 such patients with diamox and compared the diuresis with that resulting from mercurials

Diamox can lower the arterial CO_2 level, and the importance of this in the treatment of acute or chronic respiratory acidosis is at once obvious I have treated 5 emphysematous patients suffering from an acute respiratory infection and complicated by heart-failure and drowsiness, another 2 patients also had CO_2 narcosis as a result of oxygen therapy, and 2 had chronic respiratory acidosis, neither with œdema The case of the acidosis in one of them was continuous oxyg administration

During diamox therapy the diet was either salt free contained 1 g of sodium a day Initially the dosage of di was 8 to 12 mg per kg body weight daily but it was f that 250 mg twice daily was as effective and free from tox effects A single daily dose of 500 mg often caused headache and drowsiness Brachial artery puncture was done on t day before diamox was given, and on the second or third day of therapy two to three hours after the morning dose of the drug

The results are shown in the accompanying table It w be seen that there was a diuresis in those with failure due to acute respiratory infection but not in those with chron failure The 2 patients with chronic failure did howev respond to mercurials and ammonium chloride The ment state improved in only 1 patient—a man admitted becaus a respiratory infection complicated by drowsiness and hea failure Oxygen therapy produced mental confusion and sweating He was given 625 mg of diamox in a single dose in the morning and the oxygen was continued intermittently Aft three days he was fully orientated At this point the arter blood pH was 7 33, the pCO_2 79 mm, the CO_2 content 7 vols %, and the O_2 saturation 87 5% Diamox was th stopped and the arterial blood twenty four hours later show a pH of 7 42, a pCO_2 of 57 mm, a CO_2 content of 60 vols. and an O_2 saturation of 78% Two days later, still with diamox, mental clarity was retained and the blood find were pH 7 35, pCO_2 65 mm, CO_2 content 68 vols. %, O_2 saturation 90% All the samples were taken with patient breathing oxygen In view of these findings I do think that the improvement in the mental state can attributed to diamox

5 patients were adversely affected by the drug is not surprising, for, although the arterial CO_2 was usu reduced, the pCO_2 was not significantly lowered indeed was often raised Nadell[3] reported well of th use of diamox in 3 cases of respiratory acidosis In case she states that the drowsiness, cured by diam returned seven days after the drug had been discontin From the data it is seen that this change was assoc with a fall in pH and a rise in CO_2 and that on resump of the drug the pH rose and the CO_2 and pCO_2 Observations that I have made of similar events occur under similar circumstances in patients not rece diamox lead me to believe that the fluctuations in mental state are related to abrupt changes in the ar saturation rather than to the effects of diamox

Messrs Lederle kindly supplied the diamox used in investigation

Chase Farm Hospital, Enfield THOMAS SIMPSO

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1 Schwartz, W B, Relman, A S, Leaf A *Ann intern Med* 1955 42, 79

2 Nadell, J *J clin Invest* 1952, 52, 622

EFFECT OF DIAMOX IN CARDIAC FAILURE, CO_2 NARCOSIS, AND RESPIRATORY ACIDOSIS

Arterial blood						Diuresis	Diuresis from Mersalyl	Mental state	Effect on mental state	Toxic
pH		pCO_2 (mm Hg)		CO_2 content (vols %)						
Before	After	Before	After	Before	After					
Acute cardiac failure										
7 34	7 23	59	65 5	60	52	7 lb in 4 days	Good			Nil
7 39	7 23	59	68	68	57	Nil	Nil			Nil
Chronic cardiac failure										
7 37	7 30	50	55	60	53	Nil	Good			Headache
7 34	7 28	53	61	56	56	Nil	Good			Drows
Acute cardiac failure and mental symptoms										
7 35	7 28	65	69	61	57	7 lb in 6 days	Not given	Very drowsy	Nil	Nil
	7 29		64	62 5	59	net gain of 5 lb	Not given	Disorientated	Nil	Nil
	7 21		59	59	47	4 lb in 4 days	Not given	Drowsy	Nil	Nil
7 39	7 25	53	51	58	42	3 lb in 2 days	Not given	Drowsy	Nil	Nil
7 41	7 36	48	46	55	49	1½ lb in 3 days	Nil	Drowsy	Nil	Nil
CO_2 narcosis due to oxygen therapy										
7 26	7 33	94	79	85	78			Irrational	Improved	Headac
								Coma	Nil	
Chronic respiratory acidosis										
7 36	7 28	68	61	73	55			Drowsy	Nil	Very dr
[illegible]	7 29	60	71 5	65	66 5			Drowsy	Nil	Nil

RADIOLOGY OF PLACENTA PRÆVIA

Sir,—I agree entirely with Dr Russell and Dr arrick (April 16) regarding the importance of the liological demonstration of anterior placenta prævia only "difference" with them, if such it can be called, in the modesty of their claim for not only is it ssible to infer the site of the low anterior placenta wadays, radiologically but it should be possible in arly every case (after 32 weeks) to estimate the *degree* extension of the placenta on to the lower uterine gment Furthermore with increasing technical pre sion in the radiography of these cases, it becomes creasingly possible to go further and to show *factually* a number of patients (approximately 30%) the acental outline by revealing placental calcification his is a real advance fact in place of radiological pinion in this very important type of case

It should be recognised however that there is another mportant demand for precise localisation of the placenta and I always mention the placental site even if I have ot been asked to do so)—and that is in breech presenta ions, for separation of the anterior placenta *can* occur s a result of manipulation during attempts to perform ersion. Clearly in this case the danger to the fœtal ife-line is great—but the chance of the obstetrician to ave the fœtus may be less than in placenta prævia ases simply because it may be too late to do anything about it by the time recognition of the tragedy has ccurred.

Therefore I wish to join Dr Russell and Dr Warrick n their appreciation of the grand example which Frank Reid has set before the radiologists of this country in this atter of estimating the placental site accurately

St. Mary's Hospitals
Manchester 13.

J Blair Hartley

INTRINSIC FACTOR

Sir,—Mr O'Brien and his colleagues [1] have carried out n excellent piece of work in being the first to isolate an pparently homogeneous intrinsic factor substance from uman sources

I do not however find it surprising that the molecular eight is so different from that of our own material[2] hich was isolated from pig mucosa Using normal and strectomised rats in a study of the absorption of radio tive B_{12} results have been obtained which indicate at "intrinsic factor probably has some degree of ecies specificity These observations are not yet pub hed and have been carried out in collaboration with y colleagues Mr C G Clayton and Dr B Schofield ey have already been briefly reported.[3] Similar observa ons have been made in relation to animal nutrition[4] idence is therefore accumulating which indicates that number of different intrinsic factors occur in Nature state of affairs in some way paralleled by the blood oup substances which are also mucoproteins It is parently quite fortuitous that pig mucosa has proved ective in human patients suffering from pernicious mia

Although I feel these observations are adequate explain the difference in molecular weight it is uch more difficult to draw conclusions about the fference in biological activity It would indeed be rprising if pig intrinsic factor proved to be more active an human intrinsic factor in the human being Whilst agree with the possibility that the human material lated may be an intrinsic factor precursor I think one t seriously consider the likelihood that there has en some degree of biological inactivation Such partial inactivation does not necessarily affect the physico chemical tests for protein homogeneity It is not beyond the realms of possibility that it might have been brought about during the conditions associated with the operation the anæsthetic might be one possible factor

Department of Pathology
Royal Victoria Infirmary
Newcastle upon Tyne.

A L Latner.

POLIOMYELITIS NEONATORUM

Sir,—Dr Twining McMath (March 26) may be correct in considering paralytic poliomyelitis neonatorum a rare disease He will find in the *Monthly Bulletin of the Ministry of Health and the Public Health Laboratory Service* for August 1953 a full and interesting review, with 32 references, of Poliomyelitis in Infancy, Especially in the Neonatal Period by Dr J T C. Sims Roberts and Dr D Thomson Their paper includes an account of an outbreak in a private maternity home of 13 lying in beds in which 4 newborn infants were affected developing the illness thirteen twelve ten and eighteen days after birth The first 3 died in six one and two days respectively and the 4th had paralysis of the left arm The diagnosis in each case was confirmed by laboratory findings and type-3 virus appeared to be responsible

Department of Pathology
General Hospital,
West Hartlepool,
co Durham.

R T Cooke

EFFECT OF ANÆSTHESIA ON CARDIAC IRREGULARITIES

Sir —We have been investigating the electrocardio graphic changes during induction of anæsthesia, and Dr Barnard's letter of April 16 has encouraged us to give a brief preliminary account of some observations on trichlorethylene

An unselected group of 20 adult patients undergoing E.N.T surgery were premedicated with Omnopon and scopolamine E.C.G recordings were begun in the anæsthetic room and then sodium thiopentone (300–500 mg) was followed by nitrous oxide oxygen and trichlorethylene from a Boyle's machine This was continued for 10 minutes with the trichlorethylene lever at the on position A further dose of 200 mg thio pentone was followed by intubation. The E.C.G results during this period are summarised as follows (3 patients showed more than 1 effect):

Group I (unchanged)	1
Group II (vagal effects)	9
Group III (T-wave changes)	11
Group IV (Q R S-changes)	2

It is with group III that we are concerned here In 8 cases the shape of the T waves changed during anæs thesia suggesting that the pattern *before* induction was abnormal possibly because of apprehension, and became normal after thiopentone and trichlorethylene

No doubt T wave abnormalities are common prior to induction and disappear with anæsthesia but we shall be interested to know if others have observed cardiac disturbances abolished during trichlorethylene administration

London E.C.1

Robert I W Ballantine
Ian Jackson
B G Wells

Sir,—I was interested in Dr Barnard's report of a patient with auricular fibrillation whose heart returned to normal rhythm after an anæsthetic technique incor porating trichlorethylene Since beginning to work on the effects of this drug in 1930, I have used it on a large number of patients suffering from thyrotoxicosis with auricular fibrillation for partial thyroidectomy, and in a considerable proportion a normal rhythm returned before the end of the operation, and was often permanent These patients were premedicated either with rectal paraldehyde and hypodermic scopolamine or with pethidine and scopolamine, none was given atropine and few had had digitalis within a week of operation, so that these factors suggested by Dr Barnard can be eliminated The removal of thyroid tissue could also have had no effect at this stage My impression is that *any* type of general anæsthesia except chloroform and cyclopropane tends to abolish auricular fibrillation, although paradoxically it may initiate arrythmias in patients with a normal cardiac rhythm

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[1] O'Brien, J R. L., Taylor W H., Turnbull A L. Witts, L. J *Lancet* April 23 1955 p 84

[2] Latner A L., Merrills R. J., Raine L. *Ibid* 1954 i 497

[3] Latner A L. Biochemical Society Symposium on Vitamin B_{12} 1955 (in the press).

[4] Coates M. E. Ford J E. *Ibid*

Department of Anæsthesia
St Bartholomew's Hospital,
London, E C 1

C LANGTON HEWER

SANATORIA

SIR,—This correspondence has underlined the wide divergence of opinions held by most sanatorium physicians on the one hand and most chest-clinic consultants on the other In this problem, as in so many others, there is no hard-and-fast yes or-no answer The pattern of the disease itself is changing and hence the methods of management change From the beginning of the century, the cry has constantly been heard that the solution to the tuberculosis problem is within sight It is true that the mortality-rate from the disease has progressively declined, but that decline apparently started even before the discovery of the tubercle bacillus Yet perhaps it is more true today than it was ten years ago that the next ten years may show a considerable change in the epidemiology of the disease, which may well involve a considerable reduction in the number of beds required in the country

That many patients with active pulmonary tuberculosis can be adequately treated at home, has now become accepted as almost axiomatic There are, however, still several reasons for the maintenance of sanatoria which qualify this statement The first one is that domiciliary treatment is only possible where the home surroundings are entirely suitable, and when these conditions do not exist, the patient must be nursed in a sanatorium

Whatever may be the future developments in the epidemic nature of the disease, there is no evidence that our present methods of treatment of pulmonary tuberculosis result in a cure—as "cure" is understood in relation to other infectious diseases such as the pneumococcal and streptococcal infections It is more than likely that the tendency to relapse will persist, and under these circumstances it is still essential that the tuberculous patient should be taught to live with his disease It is this one great and essential quality of education of the patient, in the management of his own affairs and of his own particular tuberculous disease, that of itself justifies the maintenance of sanatoria in any scheme for the management of tuberculosis

The programme of education must include not only instruction from the medical and nursing staff, but also an active assimilation of knowledge by the patient himself, from the precept and example of the staff and the other patients around him And it is clear that this is one important factor which cannot adequately be provided by domiciliary treatment except under exceptional circumstances Whether this period of education be long or short, it is an important part of the treatment of the individual and is obviously best conducted during the early phase of treatment Frequently at this stage many patients are infective, and this may well be an added reason for maintaining such institutions with the purpose of limiting the spread of infection until it is considered that they are of little risk to others

Many sanatoria have become chest surgical centres with large thoracic surgical departments It would be difficult, even if it were considered advisable, to move these to other institutions, and this would also tend towards the maintenance of the sanatorium organisation

One of the major problems in the administration of any [illegible]erculosis scheme is the management of the chronic sputum-positive patient, particularly those who are homeless Many of these are suitable for and agree-able to a hostel type of environment This kind of patient is, however, prone to recurrent periods of relapse requiring hospital treatment, and it may be that the possibility of utilising sanatoria for the provision of both hospital and hostel accommodation for these chronic patients may not be beyond the bounds of administrative possibility

Much has been made of the argument that the chest-clinic physician should follow the progress of his patient and his family throughout the whole period of management of his illness This is a fundamental argument and would seem to be invalidated because of the separation of chest clinic and sanatoria physicians But if the policy of some of the more enlightened authorities is followed, of integrating chest clinic and sanatoria staff, then the separation is eliminated and each physician has the same opportunity of complete follow up of his own patients After all, the principle of having one physician to run an outpatient department only, and another one to be responsible only for the inpatients admitted from that department, has long ceased to function in most other branches of medicine

If, therefore, the chest clinic physician and the sanatorium physician each has his own outpatient and inpatient facilities, then I would suggest that the sanatoria which are required for the tasks which have been outlined may function more effectively and economically in the conduct of those procedur which can most effectively be carried out in sanator alone

Leeds Chest Clinic

GORDON EDWARDS

KWASHIORKOR

SIR,—For some years the English doctors who studying malnutrition among African children h chosen the word kwashiorkor to designate one of diseases they found. According to the recent book Dr Trowell and his colleagues,[1] the term kwashior is used by African tribes to name a disease found children who are weaned early because of a new pregna in the mother since the parents consider that the sec foetus will kill the first child, possibly by poisoning milk of the mother This superstition created the te kwashiorkor to indicate the precarious and unfavo able physical and psychical situation of the child wh deprived early of its mother's breast-milk

Dr Trowell and his colleagues give a new significa to the term kwashiorkor Other interpretations have b and no doubt will be, suggested, but these authors give up to date interpretation and explain that it refers to succession of facts, the most important of which is wean to this they add the overpopulation of the countries as a consequence, a keen competition for food Would tribes that coined the word agree to this social interpreta which has been accepted by other modern scientists? over population existed for as many years as the term been used?

In Mexico the Aztec tribe coined the word "tzipitl" be used for the same purpose Since then, the child falls ill due to the mother's pregnancy, and to a prem weaning, is called "chipil," according to C A Ro *Dictionary of Aztechisms*, and to F Santamaría's Ge *Dictionary of Americanisms* The term is often used to de the child's physical, social, and emotional conflict br about by a new pregnancy of the mother But among d the term has never been used to connote the various n tional states of the child, although a "tzipitl" is usually undernourished child

The words "kwashiorkor" and "tzipitl" cannot be ad for medical nomenclature just to maintain a colourful, e tradition of the tribes that invented them Outside many doctors see in this effort to preserve a strange term o differently interpreted and with so little scientific meaning nly a romantic desire to perpetuate absurd expressions of African tribes, to which Dr Trowell and his co-authors give n interpretation in the light of modern knowledge

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[1] Trowell, H C, Davis, J N P, Dean, R. F A. Kwash London, 1954

Other countries could surely find terms which would suggest rejudices and superstitions among their own peoples, and which would illustrate signs or accidents of undernutrition ut those words would have nothing to do with true scientific erminology

If nutrition means the normal process of assimilation of he food components and malnutrition is the imperfect ssimilation of these components, we have an adequate nd precise term to name an old disease of humanity which may produce different pathological pictures.

Dr. Trowell and his colleagues find the term malnutrition nsatisfactory because it does not define the type of malnutrition they insist there are many types of mal nutrition, one of which is kwashiorkor Undoubtedly there re different degrees, clinical features and pathological hanges in malnutrition, according to the stage of development of the disease, but it cannot be accepted in the light f modern knowledge that there are many types of mal nutrition. Kwashiorkor or any of the hundreds of names by hich malnutrition is known in Africa in South America, r in Asia, have the same cause—namely a deficiency of he nutrient elements whether through a fault of ingestion igestion, absorption, or assimilation.

Although terminology is important it is of small ignificance compared to the excellent study which r Trowell and his colleagues have carried out in ndernourished African children Their book is of great alue to all who are interested in this particularly urgent roblem of malnutrition We are grateful to the authors r their generous references to the Mexican work on alnutrition

Hospital Infantil,
Mexico.

FEDERICO GÓMEZ

RUPTURE OF THE DUODENAL STUMP AFTER GASTRECTOMY

SIR,—In their letter of April 16 Mr Lunn and Mr Noon scribe what is one of the commonest and certainly the st lethal, forms of intestinal obstruction that may low partial gastrectomy of the antecolic Polya type ging from the increasing number being reported in literature the condition is being recognised more ently, but even so it is difficult to diagnose since symptoms are often vague and the obstruction often partial. The particular kind reported by Lunn and n is dangerous since the vascular supply to the ent loop is embarrassed, and I therefore call atten , as I did in my two papers[1,2] on the subject to the l to close the gap between the anastomosis in front the transverse colon behind in order to prevent any he six different patterns of obstruction described in second paper Surgeons use the antecolic rather than retrocolic, reconstruction to save time but now that recognised that the gap in the former should be ed, this time-saving factor disappears since it is er to close the gap in the mesocolon made during the ocolic operation

he second most important point in Lunn and Noon's , though they do not mention it is the disadvantages he long afferent loop In order that the afferent loop herniate through the gap from right to left it must a long one say 12–18 inches though of course if gap had been closed even a long loop would not e herniated.

There are however two other dangers of the long rent loop I have published elsewhere[3] 3 cases, and e since had a 4th in which the long afferent loop r the course of time became concertinaed by adhesions producing such severe afferent-loop symptoms as to require further operation The third disadvantage is that very occasionally a long loop leads to steatorrhœa

Queen Elizabeth Hospital
Birmingham, 15

F A R. STAMMERS

THE HAIR OF THE PILONIDAL SINUS

SIR,—Although my own investigations concerning the origin of pilonidal sinuses are already in process of publication elsewhere, I should like to intervene in the controversy between Mr Patey and Professor Scarff (April 9) and Mr Weale (Jan 29 and April 16)

Mr Weale is to be congratulated on drawing attention to a method of establishing the polarity of loose hairs or hair fragments, but his finding, in seven specimens sectioned that the root ends of the hairs were directed cranially does not prove that they grow there Nor does it prove that this is the invariable arrangement I have described hairs entering a sinus tip first while still growing from follicles in the surrounding skin I have even seen a hair bent at its middle into a U-shape the apex of the U bend had entered a sinus, one end was growing from a follicle and the other was lying free externally It follows that Mr Patey and Professor Scarff's barley-corn trick (which works with my hair) cannot be the only force promoting entry Their original suggestion of a suction force which Mr Weale mentions with scorn proves to be correct, for I have demonstrated measured, and recorded it and a manometer tracing is included in my paper

If my theory is correct, hairs growing from the surrounding skin with their tips entering a sinus should be a common sight They are If Mr Weale is right, it ought to be possible to demonstrate hairs growing from undoubted follicles in a squamous epithelium at the cranial end of the sinus. It is not I have been unable to find a single illustration of such an occurrence during an extensive search of the literature

Liverpool 1°

ROGER BREARLEY

PREPARATION FOR WAR

SIR —Dr Glaister (April 16) in his devastating analysis of the emotional basis of power politics compares national (or power bloc) strivings for domination in a world of nuclear weapons to the child's fantasies of making the world conform to his desires rather than make the necessary compromise between those desires and reality It is no longer necessary to quote authorities to show what devastation must follow the use of H bombs, nor to show the inevitability of their use if they are manufactured But people follow their governments in refusing to make these facts the basis of rational thought they pretend that the facts are not there—that it is possible for the Powers to go on preparing to attack each other without ever actually doing so, to make preparations so much more terrible than the other side that it would be possible to 'win' a war and to construct a 'civil defence' which has some genuine reference to H bombs. It is pathetic and terrible to see men and women in positions of authority and trust simply running away from their moral responsibilities deceiving themselves and others into believing that there is such a thing as 'peace through strength' The French decision not to manufacture the bomb could yet be made to create the conditions in which governments might have the courage to tell their peoples that there is no longer safety in having two or three times as many H bombs as your enemy Churchmen to declare the moral degradation of preparing them and the leaders of our profession the futility of pretending that it would be possible to offer medical aid to more than a few of the survivors

Medical Association for the Prevention of War
291 Burntwood Lane London S W 17

DUNCAN LEYS

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[1] Stammers F A R. Brit J Surg 1952 40 58
[2] Stammers, F A R Ibid 1954 42 31
[3] Stammers F A R Bham med Rev 1954 18 2[illegible]3

Public Health

The Caravan Site

THE control of camping sites has perplexed the public-health authorities for so many years that it is refreshing to see an excursion from the confines of an unrelated specialty to present the point of view of a medical caravanner Whether it would be practicable or expedient to enforce the standards suggested by Mr William Hunter, F R C O G , is another matter He quite rightly points out[1] that many of the nuisances and abuses are due to the indiscriminate subletting of caravans, and he proposes that such hiring should be either prohibited or strictly controlled on selected sites The idea of segregation of the casual visitors from the owner-occupiers is an *apartheid* policy which might work to the mutual happiness of both groups, and indeed already obtains on some sites where the management need to exercise a firm control, or where the cultural outlook of the caravanners produce a natural clique pattern in the lay-out There would seem to be little chance of obtaining statutory powers to limit subletting, and even less chance of being able to enforce them

There is a better case for segregating permanent residential caravan sites from the more nomadic varieties, because a residential site really has the character of an improvised housing-estate and needs more highly organised communal facilities if it is not to degenerate too rapidly into a shanty-town slum Most local authorities look askance at the formation of such settlements, which seem to attract problem families and an endless succession of opportunists who try to use the caravans as springboards to jump the queue for priority in rehousing It is a practical defect in the Housing Act, 1936, that two years must elapse before a particular caravan can be condemned under the slum-clearance procedure It does not necessarily follow that no caravans should be used for permanent habitation They offer valuable scope to the tuberculous and the eccentrics, but for various reasons those people are perhaps better accommodated on individual isolated sites The casual visitors to isolated unlicensed sites remain an insoluble problem, since they drink water at their peril from polluted streams and dispose of their waste to endanger small private water-supplies Their education by an extended Country Code may be the only remedy

Mr Hunter is more concerned with the genuinely mobile caravanner being able to find the decencies of civilisation where he stops for the weekend, and the local residents would share his wish for their own sakes But even the more gregarious nomads vary in their requirements Many scorn the creature comforts of the luxury site to glory in their dream of Romany life and endure for a brief spell the more primitive sanitary habits of the gipsies, leaving unmistakable evidence where their caravans have rested For those who cannot do without the collective security of urban life, the fully equipped site is the answer Mr Hunter favours plenty of room between vans, space for easy version, and waterborne sanitation Refuse disposal can be easily organised, but rural water-supplies are often well below urban standards So long as there are such differing demands there will always be wide variations in sites It takes all sorts both to make a world and to tow a caravan

A well-organised site can, as Mr Hunter says, be a hygienic place which is an asset to the district, and the keynote is proper management by the site operator If the manager is worth his salt there will be no need for the sanitary inspector and the police constable to be hovering by the gate Surely it is better that the site owner should run his own business in an orderly and efficient way than to make bad laws to suit hard cases, and any law that cannot be enforced is bad A convoy of caravans can be driven straight through the law as it stands at present The uncertain interpretation of the Public Health Act, 1936, the status of the exempted organisations, and the anomalies with the planning legislation all make control a dangerous and irritating game of bluff In a recreation so diverse in character it would be very difficult to close all the loopholes Mr Hunter advocates stiffer penalties for breach of conditions attached by a local authority to the site licence, including even revocation of the licence to operate the site Such withdrawal would impose a financial penalty incommensurate with the offence—a principle that is only occasionally and reluctantly applied in English law Caravanners, site operators, and local authorities are only too conscious that we live in an imperfect world, but a code of good caravanning practice may achieve much better results in the long run than all the threats of penal reprisals and the temptations of evasion We seem to be made that way

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[1] Hunter W *Med Offr* 1955 93 179

Obituary

ROBERT DAVIES-COLLEY

C.M G , M Chir Camb , F R.C S

Mr Davies-Colley, consulting surgeon to Guy's Hospital, died on April 16 at the age of 73

He came of a well-known medical family His father, J N C Davies-Colley, was also senior surgeon to Guy's; his brother Hugh was civilian surgeon to the Cambridge Military Hospital, Aldershot, and his sister Eleanor, who died in 1934, was the first woman F R C S Robert himself was educated at Westminster School, Emmanuel College, Cambridge, and Guy's After qualifying in 1906 he held house appointments and registrarships at Guy's, later becoming lecturer in surgical pathology and curator of the museum. Meanwhile he obtained the higher surgical qualifications, taking the F R C S in 19 and proceeding to the degree of M.CHIR the following year In 19 he was appointed to the honorary staff, but his work there was soon interrupted by the outbreak of war and during 1914- he served in France and later in Mesopotamia where he was consulting surgeon to the Expeditionary Force with the rank of colonel For this work was appointed C M G in 1918 and mentioned despatches

[Barbara Davies Colley

On his return to civilian practice he took up his consulting practice again, and he also became consulting surgeon to the London County Council But Guy's remained the centre of his work and interest To the hospital, his juniors, and his friends he gave whole-hearted loyalty and in return received whole-hearted affection His chief interest was in surgical pathology which he taught well, and, though he was him little of an innovator, he performed the valuable function of the critic Hating bluff and show, he was one of those that hold fast to what is good A massive figure, with beak of a nose and shaggy eyebrows, he was very part of Guy's Outside his own hospital he was examiner for the Royal College of Surgeons, the University London, and the Society of Apothecaries

N M writes " Davies-Colley—affectionately D G always gave one the impression of a countryman whose lot Fate had cast capriciously in the city, where the fullness of time his gift commanded professional recognition and renown

" He was already a person of note at Guy's when first entered the school some 47 years ago There he initiated me into the mysteries of obstetrics and gynaecology while he was serving his apprenticeship as registrar in that department before proceeding to general surgery Between the two world wars we were colleagues on the senior staff of Guy's, and from the year of crisis 1939 association grew closer as we served together in the E M S at Farnborough, in Kent, where he was the ficient officer in charge of that decentralised unit of our parent hospital. There his lucidity of thought and simple directness of action, qualified by patience and disciplined by strict integrity stood us all in good stead as we strove to coördinate the dual control of central and county authority and reconcile their often divergent views on methods, means, and objectives He was tactful too.

"Much of his success as a surgeon was due to the acuity of his insight and to his refusal to be distracted by irrelevant detail. When his counsel was sought it was with confidence that he would advise no hazardous adventure by Surgery's wilder shores, but direct one along the safest path where lay the greatest promise of relief"

Mr Davies Colley married in 1908 Emily Cecilia daughter of Arthur Crosby-Jones There are two daughters of the marriage.

DAVID THOMAS BARRY

M D R.U.I D.Sc. N U I., F R.C.S. D P H

Professor Barry who died in London on April 15 won professional distinction in two countries In Eire he held the chair of physiology at University College, Cork, and during vacations he joined an active group of experimental physiologists in France This cross-Channel contact was of great value to him as a teacher

He was born at Ballyanihan co Cork, in 1870 and he studied medicine at Queen's College Cork, where he graduated M.B R.U.I in 1894 He spent some years in general practice at Rock Ferry, Cheshire, during which he attended courses at Liverpool University He proceeded to his M D in 1903 and the D P H in 1904 After some years of postgraduate study in London with Starling and later in Berlin and Heidelberg he took his F R.C.S in 1907 The same year he was appointed to the newly created chair of physiology in Cork at Queen's College (later renamed University College) His first task was to build up his new department which had previously been linked with the department of anatomy

During the 1914–18 war he was not released for service and he remained in Cork. In 1918 he took the D.Sc After the war he spent his vacations in France where his wife, the daughter of a Paris architect, had settled with their children Barry worked in Paris at the College de France with Gley, at the Sorbonne with A. and B Chauchard and the Lapiques, at the Institut Marey, and in Dinard at the Laboratoire Maritime In 1920 he was appointed chevalier of the Légion d Honneur

He published some 60 original papers many of which dealt with heart perfusion and electrocardiography He also condensed and translated many papers for *Physiological Abstracts* He retired from his chair in 1942

[Lafayette

A. St G H writes: David Barry was an individualist, whether scientific or social, and one whose words always *provoked thought though not* necessarily agreement. His Irish forthrightness resulted in lucid exposition of the interpretation he had put on the problem discussed whether it was the mode of contraction of the heart, the position of the Church in Science or the support of Science and Medicine in the British Isles as contrasted with the Continent. He felt deeply and sincerely, and sometimes discussion became difficult though never dull.

His studies in Heidelberg Berlin and Paris were in the tradition of the British and Irish scientists and medical men at the turn of the century

Those who examined with him will well remember his home the pleasure of meeting his wife and the sense of culture thought and generous warmth of heart which existed in that old historic home of the Bishops of Cork

Professor Barry is survived by his widow, Marie Yvonne, née Boiret, and by their two sons, Dr C T Barry and Dr D R Barry

Appointments

AYLWIN J A M.B Leeds F R.C.S.: consultant asst thoracic surgeon United Leeds Hospitals and consultant thoracic surgeon, Leeds Regional Hospital Board.

BRODDIN, PATRICK L.R.C.P I: asst county M O and school M.O Brighouse, Elland and Queensbury area, Yorkshire

CRAMMER, J G M B Glasg F.F.A R C.S. D.A consultant anæsthetist, Northallerton H.M.C

HAIGH KATHLEEN M. C. M.B Leeds D OBST: senior asst. county M.O and school M O Colne Valley Denby Dale Holmfirth Kirkburton Meltham, and Saddleworth urban district councils and the West Riding County Council

HENRY H S A. M.B. Belf, F R.C.S I, D.P.H D L.O. consultant E.N T surgeon South Down, South Armagh Banbridge and Dromore H.M.C.s

HIBBARD B M. M.B. Lond D.OBST registrar in obstetrics and gynæcology, Bath group of hospitals

HODGES H CHRISTINE, M.B. Wales D.M.R.T part time asst. radiotherapist (S H.M O) St. Mary's Hospital London

MACKENZIE, I C. K., T D., M D Camb M.R.C.P asst. physician neurological department Guy's Hospital, London

MARTIN DOREEN M., M B. Lpool M.R.C.O.G hon. asst. gynæcologist Providence Hospital St Helen's Lancs

MURPHY JOHN M.B Glasg, D.P.M psychiatrist (S H.M O) Stratheden Hospital, Cupar Fife

PARKER D S., M.B. Lond D.C H D P.H deputy M O H and school M.O Swindon.

RITCHIE, E. A A., M B Lond., M R.C.P D I.M whole time senior asst psychiatrist Rauceby Hospital Sleaford Lincs

ROSENBERG H., M.R.C.S D P M whole-time consultant psychiatrist Morgannwg Hospital, Bridgend Glamorgan.

SCOTT A G., M B. Aberd. D.P H deputy M O Norfolk County Council

SMALL, W P M.B. Edin. F R.C.S.E M.R.C.P.E consultant surgeon, Western General Hospital, Edinburgh.

WALKER N W, D.M.R.E. hon. asst. radiologist Providence Hospital, St Helen's Lancs

WALLIS E MARJORIE, M B Edin., D OBST asst M.O.H and school M O Swindon

WILLIAMS, K M. M D. Birm D.P H. D I H. principal asst M O.H. Westminster and Holborn

WILSON, J N CH.M Birm., F R.C.S. part-time consultant orthopædic surgeon, Royal National Orthopædic Hospital London.

Eastern Regional Hospital Board (Scotland):

BUCHAN ALEXANDER, M D. Aberd., F.R.C.S E. M.R.C O G asst obstetrician and gynæcologist (part time consultant) Dundee area.

MILLIKEN, J G M D. St And., D.A consultant anæsthetist Perth area.

MITCHELL, R. G M.D Edin M R.C.P.E. D C.H: asst pædiatrician (whole-time consultant), Dundee Royal Infirmary and Maryfield Hospital Dundee

Leeds Regional Hospital Board:

CHARKLEY A. D M B. Lpool: senior casualty officer Batley and Dewsbury General Hospitals

HANSELL, J L., M B Camb: whole-time asst. chest physician and deputy medical superintendent (S.H.M.O) the Hospital Grassington near Skipton.

PRATT T L C, M.R.C.S D.M.R.D whole time asst. radiologist (S.H.M.O) Huddersfield and Halifax groups

WHITE, J M. M D Glasg., D P.M whole-time consultant psychiatrist and deputy physician-superintendent Stanley Royd Hospital Wakefield

Liverpool Regional Hospital Board:

JONES O. H, M.B. Lpool: whole time asst pathologist Alder Hey Children's Hospital Liverpool.

RICHARDSON, J C., M B. Lpool F F.A R.C.S., D.A. consultant anæsthetist Liverpool city area

WALKER G D D.M Oxfd M.R.C.P whole-time consultant physician-superintendent Newsham General Hospital Liverpool.

WALLACE JONES D R. M.B Lpool, D.M R D consultant radiologist North Liverpool and Fazakerley groups

Births, Marriages, and Deaths

BIRTHS

KAGAN.—On March 29 to Barbara and Aubrey Kagan, [illegible]—a brother (Aubrey James) for Penelope Ann and Alfred Nicholas

TASKER.—On April 14 at Northampton to Anita wife of Dr J R. Tasker—a daughter

DEATHS

BARRY.—On April 15 David Thomas Barry M.D D.Sc., F R.C.S., D P H., chevalier de la Légion d Honneur emeritus professor of physiology University College Cork of 7 Lancaster Gate W 2 aged 84 R.I.P.

Notes and News

THE WEST END HOSPITAL

Many hospitals were heavily damaged during air attacks in the late war, but the West End Hospital for Neurology and Neurosurgery (as it is now called) in London was particularly hard hit In 1940 the outpatient department in Welbeck Street was struck by a bomb and a nurse was killed A fortnight later a land mine fell in the grounds of the inpatient department in Regent's Park Happily there were no casualties, but the building was badly shattered It was repaired, only to suffer even more severely in 1944 when a flying bomb killed eleven patients and one nurse, and a second nurse lost her sight Despite these blows, the hospital's work (like so many other important features of the nation's life) went on. Beds were lent by various other hospitals, and after the war, in 1946, a neurological unit of 60 beds was set up at St Charles's Hospital, Ladbroke Grove, and this is still in action

With the coming of the National Health Service, the future of the hospital was discussed, and it was finally decided that the premises in Dean Street so long occupied by the London Lock Hospital should be reconstructed as new (and now combined) inpatient and outpatient departments of the West End Hospital And the culmination of this plan has now been marked by a reception held in the newly fitted outpatient hall in Dean Street on April 22 Extensive reconstruction has met all the complex needs of a modern neurological hospital, and it was clear to guests at the ceremony that the hospital staff are looking forward to the opportunity of providing, in their new home, an even finer service than at any time in the hospital's distinguished record, which began in 1878

There will be about 40 beds to begin with, but there is room for expansion Wards have been named after the nurses who were killed or gravely injured during the bombing The department of speech therapy which has long been associated with the hospital will carry on its work and so will the School of Speech Therapy Various special departments are attached to the hospital, such as dermatology, orthopædics, ophthalmology, and otorhinolaryngology, so that the neurological consultants will have ready access to colleagues in these specialties But the extensive psychiatric and child guidance departments, which had grown very large (too large, many thought, in relation to the size of the hospital as a whole), will in future work independently as the St Marylebone Hospital for Psychiatry and Child Guidance, in Cosway Street, off Marylebone Road

At the reception Dr T Rowland Hill, physician to the hospital, welcomed as its new patron, Lord Bruntisfield, and he spoke warmly of Lord Bruntisfield's considerable services to the hospital in the past, particularly during adverse times Dr Rowland Hill hoped that the hospital, now that it had recovered from its wartime setbacks, would expand still further in the future Meanwhile, he felt that the new building would give an impetus to even better achievements in neurology and neurosurgery

THE INWARD EYE

Most of us, as the years go by, learn to take new experiences with a certain fortitude But this by no means always applies to æsthetic experiences, and many people are profoundly disturbed by unexpected sounds in music and unexpected methods or subjects in painting and sculpture Art critics have their work cut out to interpret to each succeeding generation the new forms which the musicians and painters are trying to explore

Perhaps it is true that, as Eric Newton said recently in a broadcast,[1] few of us can read a picture as easily as we read a poem we are not visually literate, and cannot hope to be, for whereas we practise talking, reading, and writing—some of us for many hours a day—few of us ever practise painting at all Moreover we, in this generation, are perhaps confronted, with special difficulties, for many artists have given up representing the visible world in a relatively straightforward way, and are instead concerning themselves with abstractions such as emotions and the contents of the unconscious mind Why not ? They have as much right to unconscious minds as other people and at least as much right as psychiatrists to explore them It does mean, however, that we must take a little trouble to follow their symbols just as it took a little trouble to follow the symbols in, say, T S Eliot's *The Waste Land* This at least, is the opinion of George Wingfield Digby, whose new book, *Meaning and Symbol*,[2] interprets the work of three modern artists—Edward Munch, Henry Moore, and Paul Nash—in terms of Jungian psychiatry

Munch, deeply introverted and depressed, painted pictures which have their counterpart (in content if not in skill) in the paintings of many mentally ill patients in hospital. They often reveal an oppressive universe, his own fear of it and the division he found in his own personality Thus his portrait of himself in an almost deserted restaurant shows, towards the back of the room, a pair of waiters—or perhaps one waiter split in two, the halves standing back to back In *The Fight* two figures, one black one white, prepare for conflict, and in *Unwelcome Guests* he has taken up his gun to shoot, through the window, his black and white doppelgängers as they approach his house His emotional perturbation, like that of Edgar Allen Poe, informs all his work but his skill and power as a painter allow him to use it resourcefully, with beauty

Very different in feeling is the work of Henry Moore, whose vast stone forms of women, generous, mindless fertile are part of the mindless fertile earth out of which they seem to grow He finds in natural rocks, weathered and pierced with smooth holes, a poetic expression of life and change, and he gives to his material much more freedom than sculptors have been wont to do, allowing it "to reduce and assimilate the human character of the form into its own material nature" Digby suggests that archetypal themes of death and rebirth, the dismemberment of Osiris and of Dionysus, and many other echoes from mythology are also to be found in his work

Paul Nash, too, was engrossed by Nature—by the seasons, by strange encounters of natural and man made objects, and, like both Eliot and Moore, by the splendour and generosity of fertility Many of his symbols are as direct and unsubtle as fertility itself—the sunflower, bearer of thousands at a generation the serpent whose head is so often shown piercing the sun's disc, the phœnix springing from a cavernous nest, the convolvulus, the mushroom, the sun itself

To appreciate an artist's symbols is to get rid of a good deal of unconscious hostility, for until we can speak his language he is one of these damned foreigners, and the inward reflection "Can't understand what the fellow's getting at," finds outward expression in "Why can t he talk sense?" But once the secret is out, the language learnt, we warm to him, and are free to enjoy his work And really the trouble required is not very great, for as Digby says, "the expression of an artist who can reach down to the fundamental in human is never as complicated as our thinking processes make it appear, it is usually only difficult to his immediate contemporaries"

CENTRAL MIDWIVES BOARD

The following have been appointed as members of the board for the next three years

Appointed by the Minister of Health —Miss G M Godden O.B.E. S R N, S C M matron, Hammersmith Hospital I G Innes M.D. general practitioner Hull G T Milne assistant secretary Ministry of Health J A. Scott O B E M D medical officer of health, London County Council, Miss V R Shand S R.N, S.C.M. M T D supervisor of midwives Lancashire County Council Arnold L Walker C.B E. F R C.S F.R.C O G casualty obstetrical surgeon City of London Maternity Hospital (chairman)

Appointed by the Royal College of Physicians —Alan A Moncrieff C B E M.D F R.C P Nuffield professor of child health, University of London (vice-chairman)

Appointed by the Royal College of Surgeons —A M Claye F.R.C.S. F R C O G, professor of obstetrics and gynæcology, University of Leeds

Appointed by the Royal College of Obstetricians and Gynaecologists —Victor Lack, F R C.P F R C.S F R.C O G, obstetrical and gynæcological surgeon London Hospital

Appointed by the Society of Medical Officers of Health —Miss Jean Mackintosh M.D senior administrative medical officer Birmingham

Appointed by the Royal College of Midwives —Miss E K Hill S R N S C M M T D supervisor of midwives Holland County Council Miss M I Farrer S.R.N S C M M T D, D N (Lond) matron St Mary s Maternity Hospital Croydon Miss E J Merry S R.N S C.M, general superintendent Queen's Institute of District Nursing Miss M Williams, S.R.N, S C.M, M T D matron Queen Charlotte s Hospital

Appointed by the County Councils Association —A Elliott M.D medical officer of health Kent

Appointed by the Association of Municipal Corporations —Alderman F E Tylecote M D F R.C.P, professor emeritus of medicine University of Manchester

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[1] *Listener* March 10, 1955 p 424

[2] London Faber & Faber 1955 Pp 204 30s

EMPIRE RHEUMATISM COUNCIL

In his report to the annual meeting of the Empire Rheumatism Council in London on April 27 Dr W S C Copeman, the chairman said that the Council s record of achievement in 1953-54 was one of which they could justly be proud Their views on the recognition of rheumatology as a specialty had been put before the Minister of Health who had promised that in the new Ministry circular dealing with senior appointments, rheumatology would be mentioned as a subject in which a senior medical registrar could be employed during his training The Council judged this to be an important advance

In the past year an all-out effort had been made to increase the Council's finances, and Dr Copeman referred to many generous contributions, and particularly to the heartening response to the appeal launched last October at a dinner at the Mansion House which was attended by the Council s president the Duke of Gloucester

The financial report shows an income for 1953-54 of £16 723 (exclusive of legacies) compared with £10 019 in the previous year Medical expenditure on research work totalled £10 151 as against £8128 in 1952-53

IMPERIAL CANCER RESEARCH FUND

The Fund s annual general meeting was held in London on April 28 In the report on its affairs in 1954-55 the treasurer Mr A Dickson Wright records a further considerable increase in the number of subscribers to the Fund Receipts from subscriptions and donations amounted to £22,880 and from investments to £41 507 Legacies totalled £118,542. Dr James Craigie F.R.S director of the central laboratories at Mill Hill summarises the many pieces of research that are going on there He observes that the inter relationships between many aspects of the work are increasing The clinicopathological research unit, directed by Prof Geoffrey Hadfield at 48 Lincoln s Inn Fields, is finding its quarters much too meagre for the sizeable plans it has in mind, and an offer from the Royal College of Surgeons for the use of two nearby sites has been accepted As soon as the College is able to vacate these buildings, the sites will be let to the Fund, with the right to demolish the existing houses and rebuild.

University of London

Mr G B West D.SC lecturer in pharmacology in the University of St. Andrews, has been appointed to the readership in pharmacology at the School of Pharmacy

The following degrees have recently been awarded by the senate :

M.S—D J Robertson.
Ph.D (*in the faculty of medicine*)—T W Glenister M C Lancaster Khagendra Chandra Basu Mallik.

National University of Ireland

The degree of M.D has been awarded to Brendan O Mordha.

Society of Apothecaries of London

At a recent examination for the L.M.S.S.A The following were successful

R. A. Norton F Heyes A D Scott M. E. Khan G K Gregory A. W L Beatson, A G Day K G Mellish Oxley R A Greig A. W Prentice J G Teall, M. A A M Pelosi D Lyen, D Procter

Royal College of Physicians of Edinburgh

Dr Jessie Macgregor Prize for Medical Women (£75)—An award of this prize will be made in July for original work in the science of medicine Such work may be published or unpublished but must not have been published earlier than July 1951 It is open to women who are graduates in medicine of the University of Edinburgh or who have taken the Scottish triple qualification. Applications must reach the convener of trustees at the college 9 Queen Street Edinburgh 2 not later than June 30

Health Centres and General Practice

A debate on the rôle of health centres in the general practice of the future will be held by the Sigerist Society at 3 P.M on Sunday May 8, at 45 Russell Square London W C.1 Dr Hugh Faulkner will explain why he thinks a general development of health centres should benefit both patient and doctor and Dr Stephen Taylor will present his criticisms and his alternative. The meeting is open to non members of the society

Royal College of Surgeons of England

At a meeting of the council on April 21, with Sir Harry Platt the president in the chair honorary fellowships were conferred on Mr William Doolin (Dublin) and Prof Robert Janes (Toronto) The following were elected to the fellowship without examination as medical practitioners of at least 20 years standing Mr R D Langdale Kelham (Roehampton) Mr L S Debenham (Scarborough) Prof J McCunn (Royal Veterinary College) Mrs E L G Hilton (University College Hospital) Prof G J Cunningham was admitted as Sir William Collins professor of human and comparative pathology and conservator of the pathological museum

The Jacksonian prize for 1954 was awarded to Mr Cecil W D Lewis, and a certificate of honourable mention to Dr Oliver C Lloyd The council selected Portal Hypertension as the subject for the Jacksonian prize for 1956 The John Hunter medal and triennial prize was awarded to Stephen L Baker and the Mitchiner medal for 1955 to Colonel W R M. Drew

A diploma of membership was granted to Barbara Y Stockhausen. Diplomas were granted jointly with the Royal College of Physicians to the following :

D C H—Phyllis B Banks Rosalind A Barnes, Yvonne G Beeching Maurice Berger R. J Burns Alison M. Bush Abdul Hamid Ismail Bustani R J Cantwell Shireen H Captain Verne Caradus Marie D Carroll Delsya R. Conway A T Cook Josephine Cook, M J F Davis Joan M Duncan, Bernice B Eldred D W Evans Joyce A Fiddick I W W Fingland J P F Fogarty Sheila M. Forbes Grace E S Forrest, Isobel D M. Forster Nirmala H Gopaldas Audrey Greenberg Sheila M Griffiths Jean M. Halliwell, Christine E E Hammond Heather S Hardcastle Felicity Harris D B Hawkins J R. K Henry, Pamela F Herst Margaret Hope Shanti Indra R J Jameson, C C A Janes K. N Kanwar Daphne M. Kirkman Ethel E. A. D Knowles Ky Kyi Wain W J Laurence, S J Lazar Boris Levin Samuel Levin S E. Levin Jerzy Lissowski Margaret B Living Taylor Judith M Macdonald Silvia A M. Marshall, Moira J Martens Ann G Morgan Avisa J M Morley Sailendra Nath Mukherjee Purnendu Samaddar Mukherji R J Pott, Malathi Rajasingham T H Roach, Balasubramaniam Saraswathy Margaret Schafran Phyllis F Slator, G J R. Soutter, C F Stroud S M. Thornton Catherine J Tulloch, D J van Pletzen D H Wadelton N D Walker Benjamin Weinstein, Joan C. Wells Janet M White Kathleen M. Witham, Ponniah Yoganathan

D O—G Augustus Binns, M. E. Cameron G V Catford Nanda Kumar Chatterjee, Sakti Das Chatterjee, F. J Cherington, Mario Cortes Valda, A T Daly P B du Toit Joan E Farrar P U E. M. Forlmer C. C Grunberger J B Hickey W D Hopkins Inder Sen Jain, Mohammad Abdul Jalil L. J Lowth, Anne M. McEntegart Ruth B Mackenzie Louis Moyerson Denis O Keeffe J A. Pratt Johnson J H M Romano G K Saraf C. J Sharp B K Singh Carlos Suarez, R. D Suckling Arthur Victor

D Phys Med—R. W Barter D A Brewerton Audrey Carey R P Goulden P Hume Kendall D R L. Newton.

D T M & H—Nassif Amin Awad, A R. Bergman Gloria J Carter Ramanlal Kalidas Desai Margaret S Dawe, W J D Eberlie M A Fawkes Joseph Gatt Mohammed Abdul Ghani Gev Sorabji Godiwalla C. D H Gunaratne D D Hilton F M James, Dorabji Minocher Joshi, Kantilal Khemchand Kapadia J E. H Lahaise A J Lewis Leonard Linnell J G McKenny I M Mansoor, E. J Monteiro James Parkyn Sudhir Kumar Ray Sisir Kumar Roy W L. Sanders Khalid Asad Shami Henry Shore R O Short, Jutta Singer, Vaiyapuri Velayudhan, T G A L Warrington G C. Willis J A Wright

Association of British Pharmaceutical Industry

At the annual dinner held in London on April 20 Sir Russell Brain P.R.C.P., spoke of the medical profession s debt to the pharmaceutical industry—for its research for its day to-day service in providing what is needed for the treatment of patients, and also for the guidance which we all receive as individuals. No industry surely was faced with more complicated problems—problems inherent in the rapid changes taking place in medicine ' You may embark on some important project producing something vitally necessary at the moment and then very quickly it may all be swept away by the appearance of something fresh And in medicine added Sir Russell we are very much aware of the importance of conditions for the pharmaceutical industry in which it can continue to do its good work in promoting research and compete in the export market with any country in the world Mr J F Boucher president of the association said that of a total annual production of about £120 million, no less than £33 million is exported, which is only slightly less than the £37 million spent by the National Health Service Discussions were still going on with the Health Departments on the principles of establishing satisfactory prices for preparations placed by the Cohen Committee in categories 2, 3 and 4 This is a most difficult question and the departments and ourselves are aware that whatever is eventually agreed great care must be taken to see that our export trade and research efforts are not impaired in any way

Medical Association

The gold medal of the association has been awarded to Sir Henry Newland, a past president of the Royal Australasian College of Surgeons

British Association for the Advancement of Science

The Association's annual meeting is to be held this year in Bristol from Aug 31 to Sept 7 under the presidency of Sir Robert Robinson, F.R S Further particulars may be had from the secretary of the association, Burlington House, London, W 1

Psychosomatic Research

The first European Conference on Psychosomatic Research, held at the Maudsley Hospital on April 22–23 was attended by workers from Belgium, Denmark, Finland, France, the Netherlands, Portugal, Spain, Germany, and the United Kingdom A second conference will be held next year in Amsterdam

Poliomyelitis Research Fellowship

On April 14 the National Fund for Poliomyelitis Research announced the establishment of a fellowship, for two years in the first instance with an annual stipend of £1250, at Queen's University, Belfast (*Belfast News-Letter*, April 15, 1955) Dr D S Dane, who is at present medical research officer at the Institute of Medical and Veterinary Research, Adelaide, will be the first holder of the fellowship

World Health Assembly

United Kingdom delegates and advisers to the eighth World Health Assembly, which opens in Mexico City on May 10, will be Sir John Charles, chief medical officer, Ministry of Health, Sir Eric Pridie, chief medical officer, Colonial Office, Mr W H Boucher, Ministry of Health, Mr J F Hunt, Ministry of Health, Dr M T Morgan, Ministry of Transport and Civil Aviation, Mr A E Joll, General Register Office, Mr H T Morgan, H M. Embassy, Mexico City, Dr A A Peat, director of medical services, Trinidad, and Dr J W P Harkness, medical adviser to the development and welfare organisation, West Indies

British Association of Physical Medicine

At the annual dinner held at the Royal College of Surgeons on April 22 Sir John Charles, chief medical officer of the Ministry of Health, said that we were not the first to be troubled by the cost of medical care an illness of Edward I's, in 1307, including materials for embalming, cost the equivalent of £2000 in our money Nor were we the only people to be troubled one could hardly pick up an American journal without seeing a reference to the subject Nobody was in a better position to influence expenditure than the doctor, and none, Sir John thought, had a more important part to play than the specialist in physical medicine Insurance and the making up of wages had done much to remove people's anxiety, but, good though they were, they had an undesirable side-effect in that often, though not always, they reduced the incentive to get back to work An active and dynamic rehabilitation department could set the goal of speedy recovery A new and growing problem was that of securing the recovery of those who formerly would have succumbed to infection in the United States, it was estimated, 24% of all hospital beds are now occupied by patients over 65 years of age, and by 1970 the proportion will be 34% Rehabilitation required both a medical and a social approach, and should be a part of all clinical practice rather than a single specialty But physical medicine was responsible for the occupational and physical therapy which had so large a part in the rehabilitation of many disorders difficult to handle Rehabilitation needed team-work—the modus operandi of modern medicine, and it should be one of the major contributions of physical medicine to the National Health Service "Everyman is a potential claimant for your geriatric skill"

Lord Horder, the president, said that physical medicine was an integral part of medicine dealing with far more than residues and replacements in industry The association now had 171 members, but numbers did not mean much, and one sometimes learnt more by weighing people s heads than by counting them He wanted the association to be responsible for criteria in physical medicine if anyone was to give the Ministry or colleges guidance on what should be the qualifications for consultant status in physical medicine it should be the British Association of Physical Medicine

Sir William Gilliatt responded to the toast of The Guests proposed by Dr Hugh Burt

Diary of the Week

MAY 1 TO 7

Monday, 2nd

ROYAL SOCIETY OF MEDICINE 1, Wimpole Street W 1
8 P M *Pædiatrics* Dr Bronson Crothers (Boston) Effect
Cerebral Palsies on Growth and Development

Tuesday, 3rd

ROYAL COLLEGE OF PHYSICIANS OF LONDON Pall Mall East S W
5 P M Sir Horace Evans Certain Symptoms and Signs in Dise
of the Kidneys (First of two Croonian lectures)
UNIVERSITY COLLEGE, Gower Street, W C 1
5 15 P M Dr M. Grace Eggleton Tubular Reabsorption a
Secretion (Cushny lecture)
INSTITUTE OF CHILD HEALTH, Hospital for Sick Children, Gr
Ormond Street W C 1
5 P M Dr Bronson Crothers Methods for Neurological Apprai
in Childhood
WRIGHT FLEMING INSTITUTE OF MICROBIOLOGY St Mary's Hospi
Medical School, Paddington, W 2
5 P M Sir Zachary Cope Peculiarities of the Clinical Patholo
of Actinomyces (Almroth Wright lecture)
INSTITUTE OF DERMATOLOGY St John s Hospital Lisle Stre
W C 2
5 30 P.M Dr F R Bettley Eczema asthma Syndrome

Wednesday, 4th

ROYAL SOCIETY OF MEDICINE
5 15 P M *History of Medicine* Dr Peter Bishop Dr Addis
and his Work
8 P M *Surgery* Prof F D Moore (Boston) Prof G M Wils
Mr F W Holdsworth Endocrine Response to Trauma.
INSTITUTE OF DERMATOLOGY
5 30 P M Dr J O Oliver *Disinfection and Sterilisation.*
EUGENICS SOCIETY
5 P M (26 Portland Place W 1) Sir Cyril Burt D SC Meani
and Assessment of Intelligence (Galton lecture)
OXFORD UNIVERSITY
6 P M (Radcliffe Infirmary) Prof B G Maegraith On t
Importance of Having a Circulation.
MANCHESTER MEDICAL SOCIETY
4 15 P.M (Medical School) Dr A H Douthwaite Dr
Addiction
MEDICO CHIRURGICAL SOCIETY OF EDINBURGH
8 30 P M (18 Nicholson Street) Mr C W A Falconer Mr A
Buchan Management of Chronic Swelling and Ulcerati
of the Leg

Thursday, 5th

ROYAL COLLEGE OF PHYSICIANS OF LONDON
5 P M Sir Horace Evans Disease of the Kidneys (Second
two Croonian lectures)
ROYAL COLLEGE OF SURGEONS OF ENGLAND Lincoln's Inn Fiel
W C 2
5 30 P M Sir Clement Price Thomas Aspects of Suppurati
Disease of the Lungs
ROYAL SOCIETY OF MEDICINE
8 P M *Neurology* Group Captain W K Stewart Win
Commander H P Ruffell Smith Dr D J William
Rôle of the Nervous System in Adaptation to Hig
performance Flying
INSTITUTE OF NEUROLOGY National Hospital Queen Squa
W C 1
5 P M Dr Bronson Crothers Adaptation of the Patient a
the Family in Cases with Severe Extrapyramidal Di
turbance in Cerebral Palsy
HONYMAN GILLESPIE LECTURES
5 P M (University New Buildings Teviot Place Edinburgh
Mr E L Farquharson Early Ambulation and
Contribution to Surgery
UNIVERSITY OF ST ANDREWS Medical School Small's Wyn
Dundee
5 P M Dr A H T Robb Smith Extra Cellular Tissue in Heal
and Disease

Friday, 6th

UNIVERSITY COLLEGE
5 15 P.M Prof F R Winton Physical Factors affecting Ren
Function (Cushny lecture)
ROYAL SOCIETY OF MEDICINE
10 30 A.M *Otology* Prof Fritz Zöllner (Freiburg) Principle
of Plastic Surgery of the Sound-conducting Apparatus
2 30 P.M *Laryngology* Mr Philip Reading Mr D F N Harrison
Mr S W G Hargrove Mr C B Cartledge Oro antra
Fistula
GUY'S HOSPITAL MEDICAL SCHOOL, London Bridge S E 1
5 P M Prof J Z Young F R.S Memory Processes (Fiso
lecture)
ST MARY'S HOSPITAL MEDICAL SCHOOL, Paddington W 2
5 P M Dr Reginald Lightwood Care of the Premature Baby
INSTITUTE OF DERMATOLOGY
5 30 P M Dr R. T Brain Skin Diseases in Children
RUTHERFORD MORRISON LECTURE
5 30 P.M (Royal Victoria Infirmary Newcastle upon Tyne)
Prof Clarence Crafoord (Stockholm) Diagnosis and
Surgical Treatment of Interatrial Septal Defects

Saturday, 7th

INSTITUTE OF LARYNGOLOGY AND OTOLOGY 330 Gray s Inn Road
W C 1
NOON Professor Zöllner Diagnosis and Treatment of Tympano-
sclerosis

The Queen has approved the retirement of Lieut General Si
Alexander Hood F R.C P, as governor and commander in-chief,
Bermuda

OSTEOPOROSIS*

A. M. COOKE
D.M. Oxfd F.R.C.P
PHYSICIAN TO THE RADCLIFFE INFIRMARY OXFORD

(concluded from p 882)

The growth of normal bone and its maintenance in health in the adult depend on a number of factors—genetic, nutritional endocrine, and mechanical. I can do no more than merely mention some of these, but propose to deal in more detail with those relevant to the problem of osteoporosis.

Nutritional Defects

Nutritional defects by which the patient does not receive or absorb adequate amounts of the substances from which bone is made, or adequate amounts of the vitamins concerned in bone formation are important—and in some parts of the world common—causes of medical bone diseases Defects of alimentation include protein deficiency from starvation (Eliot and Jackson 1933) or the protein loss of nephrotic renal disease (Emerson and Beckman 1945) and pregnancy in undernourished women, all of which may result in deficient matrix formation—i.e., osteoporosis

Pregnancy even in healthy women makes considerable demands on the mother for all body constituents, notably protein, calcium and phosphorus Kesson Morris and McCutcheon (1943) compared the incidence of osteoporosis in elderly nulliparous and multiparous women 40% of those who had not borne children showed osteoporosis against 72% of those who had borne many children, and this difference was found to be statistically significant. Nordin and Roper (1955) have recently reported four cases of severe spinal osteoporosis in young women after pregnancy They regard the high level of corticosteroids in pregnancy as a possible factor but it is only right to point out that there are also high levels of œstrogen in pregnancy Those authors do not give details of the patients diets or plasma protein levels

With regard to calcium and phosphorus, Owen Irving nd Lyall (1940) in Aberdeen studied the intake of calcium 16 men aged about 70 in relation to senile osteoporosis or economic reasons the daily calcium intake ranged om 225 to 576 mg Of these 16 patients, 6 had demon trable osteoporosis. Calcium balances showed that the bjects were more or less in equilibrium on an intake of 00-300 mg daily but when given larger amounts 00-900 mg., they retained large amounts of calcium

Vinther Paulsen (1953) in Copenhagen studied 33 tients over the age of 68 (28 women and 5 men) and und that in patients with a daily calcium intake of nder 500 mg the incidence of senile osteoporosis was % whereas in those taking over 500 mg daily it was nly 14% There were similar figures for the phosphorus take His series however, was small and it may be hat the low calcium and phosphorus intakes were part a more general dietary deficiency Except in the osser deficiencies of protein and mineral intake or sorption it is doubtful if malnutrition is a common ent in the production of osteoporosis. On the other nd lack of calcium or phosphorus and/or lack of tamin D will produce osteomalacia—i e deficient lcification of matrix causing the wide osteoid seams stologically characteristic of this disease (Maxwell, Hu d Turnbull 1932, Albright Burnett Parson elfenstein and Roos 1946)

Lack of vitamin C produces the peculiar and characteristic lesions of scurvy, which include defective matrix formation and hence one variety of osteoporosis Lack of vitamin A is not concerned in the production of osteoporosis

Endocrine Factors

At least six endocrine glands influence bone growth in one way or another—namely the ovary testis para thyroid thyroid, adrenal and pituitary

As the actions of the *sex hormones* have been brought to light over the past sixty years, unexpected effects on non-sexual target organs, including the skeleton, have been discovered In 1916 Laurence and Riddle in the U S.A. found that the level of plasma phosphorus in cocks, non laying hens, and laying hens was in the ratio of 100 to 115 to 205 that is to say a laying hen shows double the plasma phosphorus content of a cock, and nearly twice as much as her non laying sister

Riddle and Reinhart (1926) investigated the serum calcium of birds and found in male doves and pigeons a constant figure of 9 0 mg per 100 ml In the female bird with resting ovaries the figure was 9 3 mg , but during ovulation it rose to the remarkable level of 19 9 mg per 100 ml Other species were investigated and it soon became apparent that the large changes in serum calcium and phosphorus were confined to birds and related to the fact that they lay eggs with calcified shells. It was next shown that, before the egg-shell is formed a huge store of calcium is laid down in the bird s long bones In fact the marrow cavity is almost obliterated by bone a process known as hyperossification (Riddle Rauch and Smith 1944) The demand for calcium while the egg-shell is being formed is astonishing—5 grammes may be transferred from the bones to the shell gland in half a day These changes are caused only by the female sex hormones and the male sex hormones have no such effects (Riddle 1942) Also, the hyperossification occurs in para thyroidectomised and hypophysectomised animals just as it does in the normal, so the effects are due solely to the œstrogens (Riddle and McDonald 1945)

Experiments with mammals showed that extended œstrogen treatment was followed by hyperossification as in birds involving an enormous increase in trabecular bone and extensive obliteration of the marrow cavities (Gardner and Pfeiffer 1938 Poumeau Delille and Fabiani 1944, Baker and Leek 1946)

The effects of œstrogens on the skeleton vary however both at different sites and in different species (Sutro and Pomerantz 1942) In mice hyperossification of the long bones is accompanied by dissolution of the pubic bones In the human being and the dove the action of œstrogens is augmented by androgens, whereas in mice the male hormone counteracts the action of the female hormone In the rat, the male sex hormone is the stimulator of bone growth and the female hormone the inhibitor I mention these facts as a reminder of the danger of general ising from the particular and from one species to another (Gardner and Pfeiffer 1943)

In man long-continued administration of œstrogens causes hyperossification as is shown by the case of a patient of 88 years who should have been osteoporotic by reason of her age But she had taken a large dose of dienœstrol (up to 6 mg daily) for over four years for the carcinoma of the breast that eventually killed her Her vertebræ were noticed by the pathologist to be even harder than those of a normal young subject and sections showed besides areas of carcinomatous infiltration areas of cancellous bone entirely free from carcinoma cells where the trabeculæ were much thicker than normal

In man the male sex hormone has the important anabolic action of causing nitrogen retention—because it stimulates the laying-down of protein in muscle and in bone matrix (Kenyon, Knowlton and Sandiford 1944)

Abridged from the Lumleian lectures for 1955 delivered before the Royal College of Physicians of London on April 19 and 21 under the title of Some Aspects of Skeletal Disease amples of lack of the sex hormones, cases have recorded of defective bone growth and osteoporosis inary gonadal insufficiency in both sexes (Albright, Smith, and Fraser 1942, Labhart and Courvoisier 1950)

Of the other endocrine glands, the action of the *parathyroid* on the bones has been extensively studied Hyperparathyroid bone disease results, inter alia, in increased osteoclastic activity, and erosion of bone with cyst formation, osteitis fibrosa generalisata It is possible to have hyperparathyroidism without noticeable bone disease, and these patients sometimes show osteoporosis of the usual spinal distribution as the earliest skeletal involvement

The effects of *thyroid* function on bone are obscure Long continued overactivity of the gland produces osteoporosis Clinical hyperthyroidism and the administration of thyroid extract to normal animals cause an increased calcium excretion (Aub, Bauer, Heath, and Ropes 1929, Albright, Bauer, and Aub 1931), but some authors believe that a diet sufficient to compensate for the increased metabolism prevents these occurrences (Smith and McLean 1938, Drill 1941) Conversely, myxœdematous patients have a diminished calcium excretion

Normal *adrenal* function is also necessary for normal bone growth The condition most studied in this respect has been Cushing's disease, where osteoporosis is common (53 out of 61 cases in the series of Eisenhardt and Thompson 1938) It is interesting to note that an old name for this disease was osteoporotic obesity, and Mooser in 1921 described and illustrated an undoubted case of Cushing's disease under the title of osteoporosis, eleven years before Cushing's description Albright, in his masterly Harvey lecture of 1942 on Cushing's syndrome, attributed these effects to the anti-anabolic action of one of the adrenal cortical hormones, thereby correctly predicting one of the chief actions of cortisone some seven years before its isolation The osteoporosis of Cushing's syndrome differs in some respects from the commoner types in that the ribs are often, and the skull sometimes, affected (Sussman and Copleman 1942) The osteogenic actions of the sex hormones are effective treatment for adrenal osteoporosis (Albright, Parson, and Bloomberg 1941), although of course the other serious features of hyperadrenalism require treatment as well

Lastly, *pituitary* hormones affect the skeleton—for example the defective bone development of pituitary dwarfs, and the characteristic overgrowth of bone in gigantism and acromegaly Acromegaly also causes osteoporosis, probably because of the hypogonadism consequent on the pituitary disease

Mechanical Factors

Of *mechanical factors, immobilisation* of the patient plays the chief part in the production of osteoporosis Indeed, immobilisation of part of the patient will produce corresponding local osteoporosis Our orthopædic colleagues are well aware of the local osteoporosis in the region of fractures, in the limbs of patients immobilised for the treatment of tuberculous joints (Sissons 1952), and in the legs of congenitally paraplegic children (Katz 1953)

It has long been known that injury of any kind is followed by increased urinary excretion of nitrogen, and the nitrogen sulphur and nitrogen-phosphorus ratios suggest muscle protein as the source (Cuthbertson 1930, 1942) Howard, Parson, Stein, Eisenberg, and Reidt (1944) found that after injury the nitrogen loss was maximal at six days, and that the patients reached nitrogen equilibrium in thirty-five days They also noted that the loss of nitrogen was greater in patients with fractures than in others with comparably severe non-osseous injuries In 6 patients the average loss was [illegible] of nitrogen, equivalent to seven kilogrammes of muscle protoplasm High protein feeding had no appreciable sparing effect on the nitrogen loss (Howard, Winternitz, Parson, Bigham, and Eisenberg 1944) As nitrogen katabolism wears off, the protein metabolism returns to normal

The nitrogen loss is paralleled by a calcium loss. Howard, Parson, and Bigham (1945) found that after fractures or operations for osteotomy, patients immobilised in plaster showed an increase in urinary calcium for months, irrespective of a high or low calcium intake The loss remained constantly high, at two and a half times the normal figure, for two months, after which it fell If the patient was allowed out of plaster and mobilised, the urinary excretion of calcium rapidly fell to normal Likewise patients with paralytic poliomyelitis have been known to lose as much as 1000 mg of calcium daily in the urine These high losses in injuries and paralysis are almost unaffected by diet, calciferol, or alkalis

At first, the negative nitrogen balance was thought to be a direct result of the injury, but there is evidence that the immobilisation itself is an important factor (Cuthbertson 1929) Deitrick, Whedon, and Shorr (1948) immobilised four healthy young men in bed with both legs in plaster of paris for six to eight weeks There was of course no injury, but the nitrogen excretion rose, and during the experimental period they lost 30–80 g of nitrogen, which is equivalent to 1–2 5 kg of muscle These subjects also showed about double the normal loss of calcium and phosphorus There were no changes in the plasma-phosphorus or plasma proteins, but the serum-calcium rose by 1 mg per 100 ml

The conclusions from these observations must be that the absence of normal stresses and strains removes some of the stimulus to bone formation by osteoblasts, while normal resorption by osteoclasts continues unchecked

To an otherwise healthy adult the immediate dangers are few restoration to normal activity is followed by retention of calcium and nitrogen, and anatomical recovery But in old subjects and children the picture is otherwise In the former there is likely to be some degree of senile osteoporosis before the injury or immobilisation, and indeed osteoporotic subjects are more liable to fractures than those not so affected Recovery in the aged, whether from incised wounds, muscle atrophy, or bone atrophy, is slower than in the young

In children, the skeletal effects of immobilisation are greater than in adults, and the metabolic upset may even be fatal The change from the normal physical activity of a child to complete rest is proportionately and absolutely greater than in the average adult Cases have been reported by Albright, Burnett, Cope, and Parson (1941), Dodd, Graubarth, and Rapoport (1950), and Halvorsen (1954)

In old patients, another condition where immobilisation may do serious harm, or even kill the patient, is extensive Paget's disease Here, for some unknown reason, bone destruction and bone formation proceed simultaneously in a patchy distribution The bone formation is mostly in the weight-bearing part of the skeleton, the spine and the legs—stimulated, no doubt, by the stresses and strains of physical activity If the patient is for any reason immobilised, bone formation is checked but resorption continues unabated These patients may have hypercalcæmia, renal damage, and what Albright has described as "chemical death" (Reifenstein and Albright 1944)

Stevenson (1952) studied 85 orthopædic patients who had been immobilised for periods varying from three months to two years, and no patient failed to show osteoporosis of all the lower limb bones Sometimes the effects of immobilisation are permanent In children, interference with epiphyseal growth may result in epiphyseal disruption and premature fusion with the diaphysis (Gill 1944) Such patients may also develop a chest deformity sustain fractures from the most minor trauma when they are mobile and develop coxa valga

Attempts have been made to determine how much exercise is required to prevent these osteoporotic troubles It seems to be surprisingly small Deitrick (1948) placed voluntarily immobilised subjects on an oscillating bed for eight to twenty hours daily The oscillation halved the calcium loss and diminished the nitrogen loss and it was deemed to do this by causing a little weight bearing on the heels by inducing slight muscular contraction and by lessening venous stagnation Deitrick found that up to ten days complete immobilisation caused no detectable physical or metabolic damage to the body but that after two or three weeks effects were manifest and might have serious results Wyse and Pattee (1954) found the tilting bed ineffective in paraplegic patients and from their extensive observations concluded that the stresses and strains necessary for the maintenance of normal bone may well be due to muscular contractions rather than mere posture

Some Landmarks

The history of spinal osteoporosis can be briefly told and for practical purposes begins with the studies of Schmorl of Dresden (Beadle 1931) who examined some 7000 spines and described clearly the pathological anatomy Previous writers had certainly described osteoporosis, but had often confused it with osteomalacia and other conditions where the bones are soft or brittle Plummer Dunlap, and Moore recorded (thyrotoxic) osteoporosis in 1928 Between 1930 and 1940 cases were reported in Germany France Denmark, and the United States of America In Great Britain a short communication was made to the Association of Physicians by Morris Kesson and Balfour in 1943 and a full paper by Burrows and Graham appeared in 1945 All these writers found the ætiology puzzling the commonest views being that age and nutritional deficiency were the chief factors

An important landmark was the paper in 1940 by Albright, Bloomberg and Smith who reported 42 cases (40 women and 2 men) aged 65 and under They remarked that no case occurred before the menopause and that several were in women whose ovaries had been removed earlier in life. They therefore inferred that what was then called idiopathic osteoporosis as opposed to senile osteoporosis was really postmenopausal osteoporosis Aware of the high serum-calcium and hyperossification that occurred in female pigeons and doves and the stimulating effects of œstrogens on bone formation in male birds, they tried œstrogen therapy on their patients This produced strongly positive calcium and phosphorus balances maximal in twenty days and continuing unabated for the ninety eight days that the treatment was given On withdrawing œstrogens there was no change for fifteen days and then a slow reversal to the findings before medication A second course of treatment again produced positive calcium and phosphorus balances. Albright and his colleagues were doubtful whether this treatment would prove to be of practical clinical value but in further papers showed that œstrogen treatment was in fact extremely effective in relieving the patient s symptoms and after a long interval in improving the X ray appearance of the bones (Albright 1947a) The first papers on œstrogen therapy published in this country were those of Scowen (1948) and Anderson (1950)

The last landmark that I would like to mention is the addition of male sex hormones to treatment It had been known for many years that testosterone had an anabolic action, produced retention of nitrogen sodium potassium phosphorus, and chloride and promoted an increase in weight and increase in muscle (Kenyon Knowlton Sandiford Koch and Lotwin 1940) It was also found to produce an increase in bone matrix and hence to be a valuable aid in the treatment of osteoporosis (Koc ially 1946, Weinmann 1950) Œstrogens and androg effective in counteracting bone atrophy from disu hal well as from hormonal deficiency (Armstrong Knowlton and Gouze 1945 Gillespie 1954)

The relationship between osteoporosis and the hormones secreted by the male and female sex glands is complicated by the presence of hormones with similar actions secreted by the adrenal cortex It is at present impossible to say what relative parts these two groups play in the metabolism of bone It has been suggested that not only do women undergo a menopause, but both sexes undergo an 'adrenopause,' and men even a 'leydigpause' (Albright 1947b)

Symptoms and Signs

The symptoms of osteoporosis vary from none at all to complete incapacity from severe pains The pains are of many types, mainly in the back radiating around the trunk radiating to the buttocks and down the legs. They are usually aggravated by movement, jarring or flexing the trunk Sometimes the pains are made worse by coughing sneezing or straining at stool suggesting a root origin but, in spite of the skeletal deformities compression of the spinal cord does not occur

The physical signs likewise vary—from none at all to gross spinal deformity The commonest finding is a shortening of the trunk giving rise to a rounded kyphosis and a transverse fold of skin across the upper abdomen (fig 5) The infolded skin is keratinised showing that the fold is of long standing and not a temporary postural phenomenon (Dent, Milne Roussak and Steiner 1953)

The X ray appearances of osteoporosis are important In advanced cases it is difficult to obtain good X ray films, because of the poor contrast between the bones and the soft tissues There is sometimes poorly defined bone texture—the so-called ground glass appearance—and sometimes there is a fainter but coarser trabecular pattern (fig 6) The longitudinal trabeculæ are more prominent than the transverse presumably because the

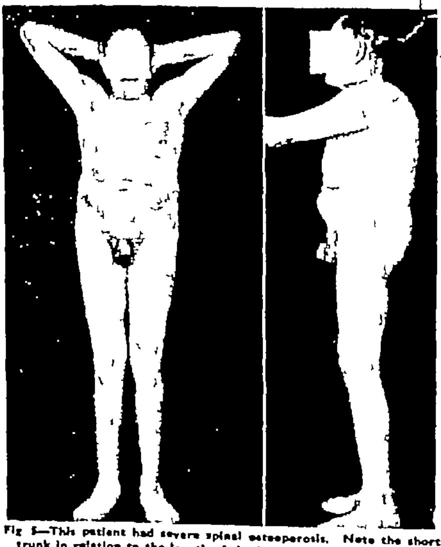


Fig 5—This patient had severe spinal osteoporosis. Note the short trunk in relation to the length of the legs the short neck rounded kyphosis, and transverse fold across the skin of the upper abdomen.

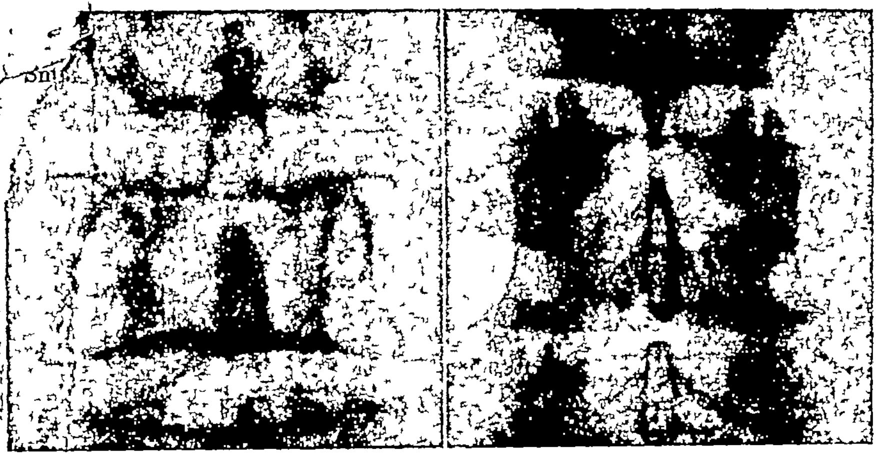


Fig 6—The normal vertebra on the right shows a fine honeycomb pattern, in contrast to the osteoporotic vertebra on the left which is less radio-opaque, and shows relatively few but coarser trabeculæ of mainly longitudinal distribution

stresses are greater up and down the spine rather than across The centra become biconcave, with increase in size in the intervertebral discs (fig 7) The centra may show denser end-plates than normal The condition is most marked in the spine, especially in the lumbar vertebræ There is a general deformity of the column, which shows a rounded kyphosis A kyphosis may, however, be due solely to disc degeneration There may be a wedge-shaped deformity of individual vertebræ All degrees of collapse occur sometimes the spinous processes become so close together that they develop false joints between them (Other decalcifying diseases, especially osteomalacia, produce similar X ray appearances in the spine, so it is unwise to make the diagnosis of osteoporosis on this one observation alone) It is usually stated that in osteoporosis the pelvis may be slightly affected, but the long bones scarcely ever and the skull almost never Actually, the other bones are affected, but less obviously so

Ghormley, Sutherland, and Pollock (1937) found that of pathological fractures arising from non-malignant conditions, one-third were due to senile osteoporosis, a cause three times as common as the next most numerous group

In patients over the age of 50 admitted to the Radcliffe Infirmary for fractured neck of femur, the condition is three times as common in women as in men It is difficult to believe that the women are submitted to more trauma than the men, and one must conclude that their bones are more brittle This belief is supported by work of Rutishauser and Dufour (1950) who examined patients who had died with fracture of the neck of the femur They cut sections of the necks of the unbroken femurs and found that these always showed characteristic changes including osteoporosis The condition is also found in the arms and legs, if the necessary predisposing factors are present and if it is sought (fig 8) These age changes also occur in compact bone as well as in cancellous bone (Amprino and Bairati 1936)

It must be admitted that the difficulties of determining the degree of osteoporosis by X ray examination are great Cobb (in Cowdry 1952) has described post-mortem chemical analyses of phalanges from patients whose hands had been radiographed during life A just-detectable X-ray difference of the dissected bone corresponded to a chemical difference of 9%, but a just detectable difference in X-ray films of the whole finger corresponded with a 25% difference in chemical analysis must be emphasised that these figures were obtained the most easily X-rayed bone in the body and in a uation where there is more bone than soft tissue Decal- spine must be even harder to detect

Similar experiments have been made by Fusi (1953) He placed complete and sliced lumbar vertebræ in 5% nitric acid, which slowly removed the mineral matter Radiological changes were visible when the isolated vertebræ had lost 3% of their calcium content, but he estimated that in the living subject changes begin to be recognisable only when the vertebræ have lost 60% of their calcium This is a surprising figure, but supporting evidence is provided by some experiments of Ardran (1951) He bored holes vertically through the centra of normal lumbar vertebræ taken from the post-mortem room A hole 3 mm in diameter could be seen clearly in a lateral X ray film of the isolated vertebra, but if the hole was filled with water it was entirely invisible A similar hole 14 mm in diameter—i e , about the size of the spinal canal—and occupying about one third of the diameter of the centrum, was naturally very obvious in an X ray film, but when it was filled with water it was only just visible as a faintly porotic area If this is so in excised vertebræ, no doubt such X-ray appearances would be even more difficult to detect in a vertebra in the body

One may therefore conclude that if there are X ray changes indicating osteoporosis, and particularly if there is vertebral collapse, there must be gross anatomical changes

The Strength of Bone

The mechanical strength of compact bone has been extensively studied, and a remarkable material it is. Its tensile strength is nearly as great as that of cast iron and its crushing strength three quarters of that of wrought iron (Bell, Cuthbertson, and Orr 1941) It is about three times as strong as wood The tensile and compressive strengths of compact bone are about equal, an unusual distinction among building materials

A vertebral centrum consists essentially of a block of cancellous bone, with a very thin outer shell of compact bone and usually weakened by a surprisingly large hole on the posterior aspect for the emissary veins

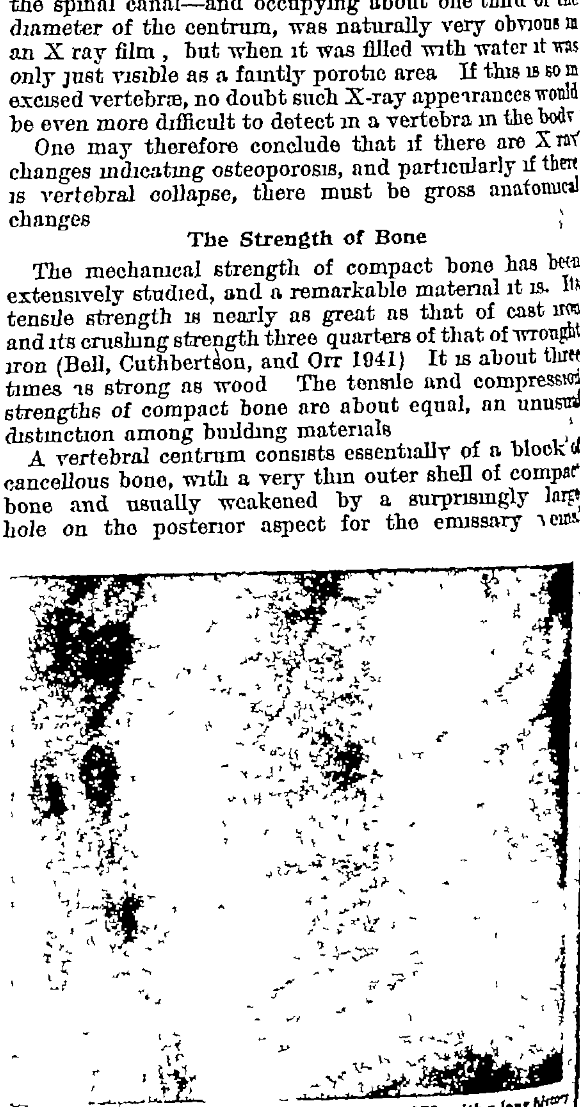
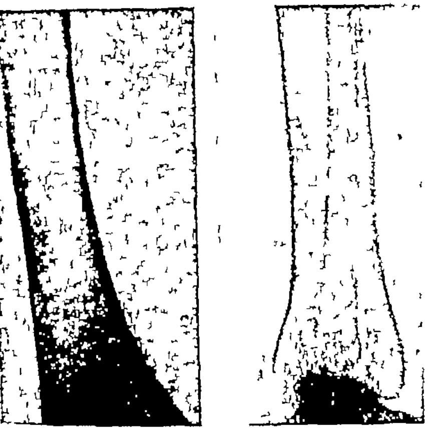


Fig 7—X ray of the thoracic spine of a woman of 73, with a long history of thyrotoxicosis and immobilisation She has a pronounced kyphosis with flattened biconcave porotic vertebræ



ig. 8 (same patient as fig 7)—X rays of (a) the lower end of the femur and (b) the lower end of the tibia.

have been able to find no modern reference to experi
ents on the strength of cancellous bone Indeed, the
ly publication is that of Ward in 1838 to whose book
have already referred He wrote:

> "A cubical inch of cancellous tissue was cut from the
> entre of the external condyle of an adult macerated femur
> nd subjected to gradually increasing pressure with the
> llowing results It sustained four hundredweight without
> isible alteration; sank a little on one side upon the addition
> the next half hundredweight and continued to yield upon
> ery further increase of pressure so that when the weight
> mounted to 6 cwt., its height was reduced to half an inch
> his reduction however took place entirely at the expense of
> e upper portion of the cube; its lower moiety which
> esented a much closer texture bore the whole pressure of
> cwt without visible alteration The weight of the cube
> bmitted to this trial was 54 grs. troy It was placed during
> e experiment in the natural position with its principal
> res upright The side on which the cube first gave way
> rresponded to the outer and posterior part of the condyle
> nd its structure was here evidently looser and more fragile
> an on the side which in the natural position had lain
> arest to the axis of the bone In Mr Rennie's experiments on
> e strength of woods a cubic inch of solid elm was crushed
> y 1284 lbs avoirdupois—about $2^1/_2$ times the weight beneath
> hich the cube of reticular tissue began to yield The com
> arison may assist the reader in forming a just estimate of the
> rength of the reticular tissue"

I have performed some similar
xperiments with the assistance
f Dr J D Todd of the School
f Engineering at Oxford which
equipped with appliances for
sting the strength of materials
riefly we found that lumbar
entra from healthy subjects
ithstood a pressure of 0 61–
67 ton (1360–1050 lb) before
ollapsing. The area of a
entrum is about 2 2 sq in
hich gives a strength of about
00 900 lb per sq in as against
he 500 lb found by Ward.
he difference was that his
pecimen was an isolated cube
f cancellous bone whereas ours
ere whole centra which have
thin layer of compact bone
around the outside and are presumably designed specially to withstand the kind of pressure that we applied

As well as the strength of 900 lb per sq in normal centra show surprising resilience even after fracture by compression When the centrum has collapsed, if pressure be increased, the deformity becomes greater until the bone is perhaps only $^1/_4$ in thick and squashed outwards till its diameter is $2^1/_2$–3 in As soon as the pressure is released, the centrum resumes its normal shape and is sufficiently strong to resist deformity by manual pressure

Osteoporotic vertebræ are easily crushed, sometimes by trauma and sometimes spontaneously or at least by the application of little more force than the weight of the upper part of the patient's body or the slight stresses caused by the muscular movements of an old person. Centra from old or osteoporotic subjects withstand a pressure of 300 lb per sq in or less, which may seem a large figure in comparison with the normal In real life, fractures in bones are seldom produced by static forces but usually by relatively small forces applied dynamically Work by Evans Lissner and Pedersen (1948) has shown that a force of only 16 inch pounds, applied dynamically to the femur can produce deformation patterns similar to those of forces of 400–700 pounds applied statically Many forms of athletics and games must produce great stresses on the skeleton but in them fractures are relatively rare because in controlled movements the muscles are used to support the skeleton. On the other hand an unexpected fall on to the outstretched hand may produce a Colles fracture with surprisingly little violence Similarly patients with osteoporosis may fracture several vertebræ from minor but sudden trauma

Diagnosis

As I have said before osteoporosis is, strictly speaking a histological diagnosis and can be made with certainty only by the morbid histologist but there are clinical features and X ray changes sufficiently well defined to justify the diagnosis at the bedside and it is an important diagnosis, because the condition is often treatable (fig 9)

In a patient over 60 years of age any pains in the trunk or legs for which there is no obvious explanation should raise in the physician's mind the possibility of osteoporosis. If the patient is a woman the chances of this being the cause are six times greater than if he is a man If there is a history of loss of height the odds in favour of the diagnosis are further increased In women special inquiry should be made about the menstrual history, the date of the menopause, and any gynæcological operations especially to ascertain whether the ovaries have been removed Questions about diet and physical activity may provide suggestive information

On examination loss of height as shown by measurement evidence of shortening of the axial skeleton a rounded kyphosis, a transverse infolding of the skin

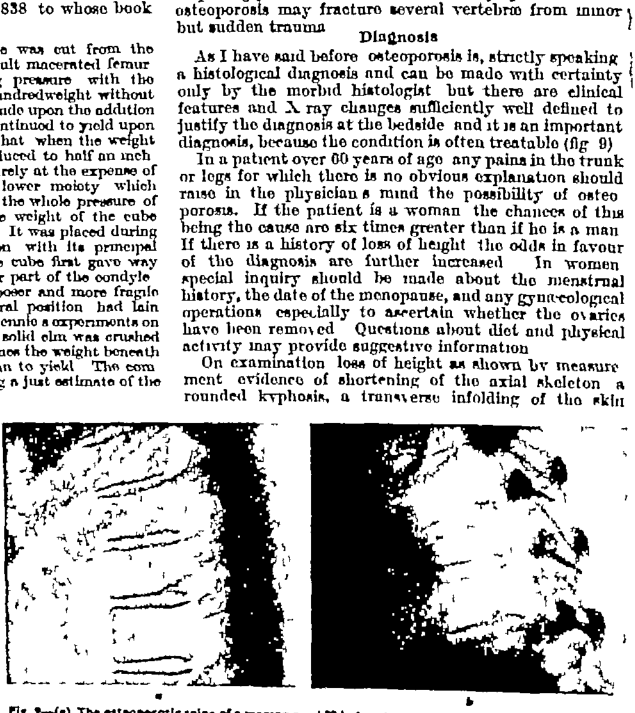


Fig 9—(a) The osteoporotic spine of a woman aged 52 before treatment. (b) The same area from the same patient (then aged 58) after 6 years treatment with calcium and vitamin D This has had no effect on the osteoporosis which has progressed and caused compression fractures

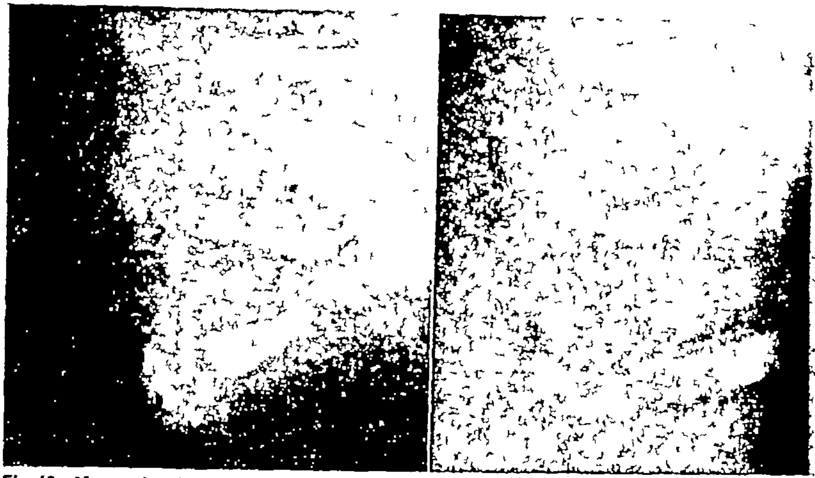


Fig 10—X rays showing radiographic improvement in osteoporosis after 2½ years hormonal therapy

across the upper abdomen, and approximation of the lowest ribs to the pelvis are important signs The patient tends to look older than her stated age, with a lax wrinkled skin Evidence of other disease will be lacking, although the thoracic deformities make the patients unduly liable to chest infections The urine should, of course, be tested for Bence Jones protein, which strongly suggests myelomatosis but is occasionally found in other generalised bone diseases Sulkowitch's reagent for the quantitative estimation of calcium in the urine provides a rough screening test for the excessive calciuria of hyperparathyroidism Radiography of the spine and pelvis will usually reveal the characteristic changes of osteoporosis, with or without fractures If there is doubt, an X ray film of the skull (which is never affected) and some of the long bones (which are rarely affected except in very advanced cases) should provide valuable negative evidence The presence of a pseudo-fracture at once raises the question of osteomalacia, in this country usually a sequel to steatorrhœa

In osteoporosis the serum calcium and phosphorus and alkaline phosphatase are within normal limits The average total plasma-proteins are in the lower normal range and the average plasma-albumin just below the lower limit of normal Basically, the diagnosis is made by the exclusion of other bone diseases Bone biopsy from the iliac crest or from the dorsal spine of a lumbar vertebra is a practicable investigation (Vogt 1949, Vogt and Tonsager 1949) Lastly, it is sometimes justifiable to try a therapeutic test

Diagnostic traps are to be found in the other diseases that produce osteoporosis as a secondary effect Cushing's disease, acromegaly, and thyrotoxicosis usually present characteristic features which should not give rise to serious difficulties More subtle and deceptive are the osteoporotic changes of myeloma, hyperparathyroidism, the osteolytic type of Paget's disease, and so called idiopathic osteoporosis The last is a rare and puzzling variety of osteoporosis occurring in young subjects of either sex, without demonstrable endocrine defect and unresponsive to hormonal treatment

Treatment

The diagnosis of senile or postmenopausal osteoporosis made, the essentials of treatment are firstly to get the patient out of bed, if only to sit up in a chair, at the earliest possible moment Secondly, if the pains are severe, a light spinal jacket will give physical and moral support Thirdly, a high protein diet and a pint of milk a day will ensure an adequate supply of the materials from which bone is formed Last, but not least, is the hormonal treatment Opinion differs on the details, but there can be no doubt that the patient needs some preparation of male sex hormone, such as testosterone propionate 10–20 mg daily by injection, or methyl testosterone 30 mg daily by mouth Androstenediol is said to have the anabolic actions without undue masculinising effect The patient also needs a female sex hormone, such as œstradiol benzoate or dipropionate 2 mg daily by injection, or an oral preparation such as dienœstrol 1 mg daily, or æthinylœstradiol 0 1 mg daily There are satisfactory proprietary preparations containing appropriate mixtures of male and female sex hormones Large doses are not required, and osteoporosis is one [illegible] diseases where twice the dose of medicine does not produce twice as good an effect, but the reverse Indeed, large doses of œstrogens inhibit bone growth Intermittent treatment will tend to prevent unpleasant side effects, and a régime of four weeks' treatment and two weeks off is often recommended Treatment should be continued for a long period, probably for not less than two years In successful cases, the trunk pains will be greatly improved in two weeks, and in severe bedridden cases in two months The effects of treatment are usually more pronounced in patients who have undergone surgical removal of the ovaries than in those who have had the normal gradual diminution of œstrogen action by age

There are many cases on record of patients with postmenopausal osteoporosis, and indeed with senile osteoporosis, who have shown great subjective improvement on endocrine therapy and a corresponding improvement in function, but very few cases have been reported where the X-ray appearances of the bone have been improved Nearly all writers on the subject comment on this curious fact

Cases of X ray improvement have been reported by Albright and Reifenstein (1948), by Sherman (19 by Snapper (1952), and by Polishuk and Kleinba (1952), and I have seen two myself (fig 10) A possible explanation is that X-ray changes for the better are seldom seen before two years' treatment and many patients are not followed up for so long a period Reifenstein and Albright (1947) estimated that osteoporotic patients receiving appropriate endocrine therapy retain about 200 mg of calcium daily If we assume that a severe osteoporotic patient has lost half the bone substance of his skeleton, which is not an excessive estimate, at this rate of replacement it would take seven or eight years to restore the bones to normal

Voltaire's gibe that "a physician is one who pours drugs of which he knows little into a body of which he knows less" is unfortunately still true and applies even to endocrinology In the treatment of osteoporosis, the chief unpleasant side effects arise from the masculinising effects of androgen therapy, which are of course most noticeable in women, who provide the majority of the patients There may be coarsening of the skin, acne, hirsutism, deepening of the voice, and occasionally unseemly increase in libido Oedema of the ankles may occur from retention of electrolytes These effects are seldom serious, but they are distressing to the patient They can best be prevented firstly by the use of small doses, secondly by intermittent treatment, and thirdly by the opposing action of œstrogens

The commonest undesired effect of œstrogen therapy is uterine bleeding in women past the menopause. Th possible carcinogenic effects of male and female sex hormones are a very remote danger because the doses are small and the drugs are merely replacing something which the patient is lacking

Prevalence

How common is osteoporosis? Omitting local forms such as osteoporosis of the pubic bone in prostatic disease Sudeck's atrophy osteoporosis cranii circumscripta, and the like over 800 cases have been reported (references in bibliography marked with an asterisk) The proportion of female to male patients was 6 to 1 and this is a significant ratio to which I shall refer later Albright has described osteoporosis as the commonest bone disease likely to be encountered by the physician Priority of place must I think, be disputed by Paget's disease but there can be no doubt that both are extremely common. It is interesting therefore to see how osteoporosis is dealt with in the standard British textbooks of medicine for students The following table shows the number of lines devoted to the subject in ten such textbooks

Textbook	*Date*	*Osteoporosis of any type*	*Postmenopausal osteoporosis*
A	1950	0	0
B	1950	4	0
C	1951	6	6
D	1952	0	0
E	1952	0	0
F	1953	4	4
G	1953	0	0
H	1953	0	0
I	1953	40	0
J	1954	8	0
	Total	62	10

A Personal Series

My own experience is similar to that of all those who have interested themselves in this condition The adult inpatient records of the Radcliffe Infirmary over the past fifteen years show that, of the common medical osteopathies there have been 110 patients with Paget's ease, 36 with spinal osteoporosis of one sort or another nd 6 with osteomalacia (all from steatorrhœa) I have so found some osteoporotic subjects among the out ttients, and with some private patients have brought e total to 50

Of these 50 patients, 43 were women and 7 men 30 ere over the age of 65, and the osteoporosis was presumbly senile in origin 20 were under 65 14 women and men, and in the women the condition was presumably ostmenopausal (fig 11)

The results of routine laboratory investigations were

	Number of observations	*Mean*
rum-calcium	37	9 5 mg per 100 ml
lasma-phosphorus	32	4 0 mg per 100 ml.
lasma phosphatase	31	9 6 units
lasma-protein	10	6 7 g per 100 ml.
lasma-albumin	10	3 7 g per 100 ml
lood sedimentation rate	26	25 mm. in 1 hour

t will be seen that the serum-calcium plasma phosphorus, nd plasma phosphatase are all within normal limits—a iagnostic point of importance The total plasma roteins are within the normal range but the plasma lbumin is just below the generally accepted lower limit f normal (4 0 g per 100 ml) The slightly raised blood dimentation rate is difficult to relate to the bone ondition because there are so many other factors which ay affect it

Apropos of the low serum-albumin levels Henneman arter, Forbes and Dempsey (1953) tried the effect of rotein administration on 4 patients with osteoporosis. here was no demonstrable effect from oral administraion Daily intravenous injections of 50 g of human rum albumin for periods of from nine to thirty days roduced a rise in serum albumin and considerable etention of calcium and phosphorus Henneman et al aferred, but could not prove that the treatment was a stimulus to bone formation and that serum albumin might 'actually be the transport form of bone matrix precursor'

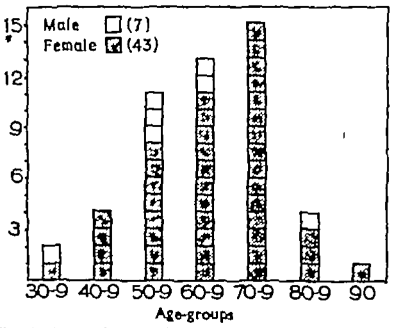


Fig. 11—Age-incidence of 50 patients with spinal osteoporosis.

Of my series 37 patients were given hormones—mostly combined œstrogen and androgen therapy—but 5 had œstrogens only and 3 androgens only The follow up was adequate in 27 cases. Of these, 1 patient said that she felt worse but the remainder reported subjective improvement in varying degrees 4 patients were able to discard plaster casts, and 2, from being completely bedridden were able to get up from bed and walk about 16 patients over the age of 65 were treated with endocrine therapy and adequately followed up Of these 15 were obviously greatly improved and 1 was the patient mentioned above who felt worse

Prevention

There is no doubt that age is a common and important factor but not as has often been supposed, the only factor It is probable that a large proportion of persons over the age of 70 have some degree of osteoporosis The fact that at all ages the ratio of women to men is six to one suggests that something other than age is operative and all the evidence points to this being an endocrine factor

It is a matter of some therapeutic importance that patients with so-called senile osteoporosis respond to the appropriate treatment for so-called postmenopausal osteoporosis. The distinction between these two types is probably not only artificial but non-existent and they are really the same disease

As regards prevention there are about 7 million postmenopausal women in England and Wales, not to mention those younger who have had the ovaries removed or irradiated and over 5 million men above the age of 50 Many persons over 50 will not of course, develop osteoporosis other than the gradual and inevitable changes which will occur if they live till 70 or over But a considerable number will sustain compression fractures of the spine either spontaneously through extreme osteoporosis or through injuries occurring on top of moderate osteoporosis and some will become bedridden and crippled A number will sustain fractures of the femoral neck from trivial injuries

This formidable problem will be met if physicians surgeons and gynæcologists have an awareness of the existence of osteoporosis and its implications and realise that it is one of the few treatable chronic conditions in elderly patients and indeed is probably the only age change in the body that can be reversed

No-one could seriously advocate universal endocrine substitution therapy after the age of 50 It would be administratively impossible and very costly and would carry hazards There are however some simple preven tive measures worth considering, specially by those responsible for the care of old people It will obviously be wise to encourage some physical activity, or at least to discourage undue inactivity It should not be difficult to arrange an adequate protein, calcium, and phosphorus intake—a pint of milk daily would guarantee 680 mg of calcium It would be simple to record the height of each subject annually, and to inspect the abdomen for the appearance of a transverse fold across the epigastrium Any aches or pains in the trunk for no good reason should at once call for antero posterior and lateral X rays

Patients with osteoporosis, or even patients potentially osteoporotic, should be given cortisone or corticotrophin with great caution, if possible not in large doses or for long periods (Hjorth and Dragsted 1953) In the recorded cases of osteoporosis with fractures occurring during cortisone treatment, the patient has almost always already qualified for osteoporosis by immobilisation or the postmenopausal state (Boland and Headley 1950, Teicher and Nelson 1952, Demartini, Grokoest, and Ragan 1952, Curtiss, Clark, and Herndon 1954)

Summary

I conclude by summarising the points which I consider the real essentials of these lectures

Firstly, the skeleton undergoes slow, steady resorption from all its surfaces, more apparent in cancellous than compact bone

Secondly, this process is counteracted by endocrine factors and the physical stresses and strains of use It is affected to a lesser extent by diet and age

Thirdly, osteoporosis is an extremely common condition

Fourthly, so called senile osteoporosis has an endocrine component which is treatable

It will have been obvious that these lectures have been largely a compilation from the work of others, whose original contributions to the subject I gratefully acknowledge I have received the most generous help from colleagues and friends too numerous to mention, but I must allow myself the pleasure of placing on record my particular indebtedness to Dr Alastair Robb Smith

BIBLIOGRAPHY

*Adams, M , Boothby, W M , Snell A M (1935–36) *Amer J Physiol* **114** 383
Albright F (1942–43) *Harvey Lect* **38** 123
— (1947*a*) *Recent Progr Hormone Res* **1**, 293
— (1947*b*) *Ann intern Med* **27**, 861
— Bauer, W Aub, J C (1931) *J clin Invest* **10**, 187
* — Bloomberg E , Smith, P H (1940) *Trans Ass Amer Phycns,* **55**, 298
* — Burnett, C H , Cope, O , Parson W (1941) *J clin Endocrin* **1**, 711
— — Parson W , Reifenstein, E C Roos, A (1946) *Medicine Baltimore,* **25** 399
* — Parson, W Bloomberg, E (1941) *J clin Endocrin* **1** 375
— Reifenstein E C jun (1948) Parathyroid Glands and Metabolic Bone Disease Baltimore
— Smith P H Fraser R (1942) *Amer J med Sci* **204** 625
* — — Richardson A M (1941) *J Amer med Ass* **116**, 2465
Amprino, R , Bairati, A (1936) *Z Zellforsch* **24**, 439
*Anderson, I A. (1950) *Quart J Med* **19** 67
Ardran, G M. (1951) *Brit J Radiol* **24** 107
Armstrong, W D (1944) *Fed Proc* **3** 201
— Knowlton, M Gonze, M (1945) *Endocrinology* **36** 313
Aub, J C , Bauer, W Heath C , Ropes, M. (1929) *J clin Invest* **7**, 97
Baker, B L Leck L H (1946) *Amer J Physiol* **147**, 522
Beadle O A (1931) *Spec Rep Ser med Res Coun Lond* no 161
Bell G H , Cuthbertson, D P , Orr, J (1941) *J Physiol* **100**, 299
Bigwood E J (1952) *Ann Rev Biochem* **21**, 355
*Black J R (1940) *Proc Mayo Clin* **15** 619
* — Ghormley R. K , Camp J D (1941) *J Amer med Ass* **117**, 2144
*Bogdonoff, M. D , Shock, N W , Parsons, J (1954) *J Gerontol* **9** 262
*Boland E W , Headley, N E (1950) *J Amer med Ass* **144** 365
*Burrows H J Graham G (1945) *Quart J Med* **14** 147
*Coboy M C (1949) *Med Ann D C* **18** 243
Cowdry E V (1952) Problems of Ageing Edited by A I Lansing Baltimore
*Curtiss P H jun. Clark, W S , Herndon, C H (1954) *J Amer med Ass* **156** 467
Cuthbertson, D P (1929) *Biochem J* **23** 1328
— (1930) *Ibid* **24**, 1214
— (1942) *Lancet* i 433
Deitrick J E (1948) *Bull N Y Acad Med* **24** 304
— W G D , Shorr E (1948) *Amer J Med* **4** 3
*Demartini F , Grokoest A W , Ragan, C (1952) *J Amer med A* **149** 750
*Dent R V Milne, M D , Roussak N J Steiner, G (1953) *Brit med J* ii 1082
*Dodd, K Graubarth H , Rapoport S (1950) *Pediatrics,* **6**, 1
*Donaldson, I A Nassim J R (1954) *Brit med J* i 129
Drill V A (1941) *Proc Soc exp Biol , N Y* **48** 448
Edelman I S , James A H , Baden H , Moore F D (19 *J clin Invest* **33** 122
Eisenhardt, L , Thompson, K W (1938) *Yale J Biol Med* **11** 59
*Elliot, M , Jackson E (1933) *Amer J Dis Child* **46** 1237
Emerson, K. jun Beckman W W (1945) *J clin Invest* **24** 54
Evans F G Lissner, H R , Pedersen, H E (1948) *Anat. Rec.* **101**, 225
*Fairbank H A T (1930) *Brit J Surg* **27**, 1
Fusi, G (1953) *Radiol Clin* **22** 123
Gardner W U , Pfeiffer C A (1938) *Proc Soc. exp Biol., N Y* **38** 599
— — (1943) *Physiol Rev* **23** 139
*Gerth (1930) *Virchows Arch* **277** 311
Ghormley, R K Sutherland, C G , Pollock, G A. (1937) *J Amer med Ass* **109**, 2111
Gill G G (1944) *J Bone Jt Surg* **26** 272
Gillespie J A (1954) *J Endocrin* **11** 66
*Golden R., Abbott, H (1933) *Amer J Roentgenol* **30** 641
Govaerts J Dallemagne M. J (1948) *Nature Lond* **161**, 97
Greenberg D M (1939) *Ann Rev Biochem* **8** 269
Halvorsen, S (1954) *Acta med scand* **149** 401
Ham A W (1934) *J Amer dent Ass* **21** 3
— (1952) *J Bone Jt Surg* **34A** 701
— (1953) Histology Philadelphia
*Hart, G M (1950) *Geriatrics* **5**, 321
Hassall A H (1849) The Microscopic Anatomy of the Hum Body in Health and Disease London 2 vols
Havers, C (1691) Osteologia Nova, or Some New Observations the Bone London
*Henneman, P H Bartter F C , Forbes A P Dempsey E F (1953) *J clin Invest* **32** 574
*Hernberg, C A (1952) *Acta med scand* **143** 1
Hevesy G C (1940) *Ann Rev Biochem* **9** 641
— Levi, H B , Rebbe, O H (1940) *Biochem J* **34** 532
Hjorth N , Dragsted P J (1953) *Acta med scand* suppl. no 2 p 33
Howard, J E Parson W , Bigham R S jun (1945) *Bull. Joh Hopk Hosp* **77** 291
— — Stein K E Eisenberg H Reidt V (1941) *Ibid,* **75**, 1
— Winternitz, J , Parson W , Bigham R S jun Eisenberg (1944) *Ibid* p 209
*Howard R P (1950) *Canad med Ass J* **63**, 258
Huggins, C (1937) *Physiol Rev* **17** 110
Ingalls N W (1931) *Amer J Anat* **48** 45
Jowsey J Owen M., Vaughan, J (1953) *Brit J exp Path* **34**, 6
*Junghanns H (1932) *Röntgenpraxis* **4** 97
Katz J F (1953) *J Bone Jt Surg* **35A** 220
*Kehoe E L , Hagan, W H (1940) *Bol Ass méd Puerto R* **41** 80
Kenyon A T Knowlton K , Sandiford I (1944) *Ann intern M* **20**, 632
— — — Koch F C , Lotwin, G (1940) *Endocrinology* **26**,
*Kesson C M , Morris N McCutcheon A (1943) *Ann rheum* **6**, 146
Koch J C (1917) *Amer J Anat* **21** 177
Kochakian C D (1946) *Vitam & Horm* **4** 256
*Labhart A , Courvoisier B (1950) *Helv med acta,* **17** 475
Lacroix P (1951) The Organization of Bones Translated S Gilder London
*Lance M , Girard L Lance P (1938) *Rev Orthopéd* **25** 385
Laurence, J V , Riddle O (1916) *Amer J Physiol* **41** 430
Leblond C P , Wilkinson G W Bélanger L F Robichon (1950) *Amer J Anat* **86** 289
*Lescher G , Robb Smith A H T (1935) *Quart J Med* **4**, 2
Logan M A (1940) *Physiol Rev* **20** 522
*Mackenzie, D A Janes J M (1954) *Canad med Ass J* **71** 339
*Marum G J (1946) *Radiology,* **46**, 220
Maxwell J P , Hu, C H , Turnbull, H M (1932) *J Path* **35** 419
*Means J H , Hertz, S , Lerman J (1937) *Ann intern Med* **11**, 1
*Merklen P (1936) *Gazz Osp Clin* **57** 1189
*Meulengracht E (1939) *Acta med scand* **101** 138 157, 187
*Michon P , Lochard, Mme Gaussin (1948) *Rev méd Nancy,* 143
Miller, H Wilson G M (1953) *Clin Sci* **12** 97
*Moehlig R C Adler, S (1947) *Surg Gynec Obstet* **64**, 747
Mooser H (1921) *Virchows Arch* **229** 247
*Morris N Kesson C M., Balfour B A (1943) *Quart J* **12** 263
Murray P D F (1936) Bones A study of the Development Structure of the Vertebrate Skeleton Cambridge
— Huxley J S (1925) *J Anat Lond* **59** 379
*Nathanson L , Lewitan A (1941) *Amer J Roentgenol* **46**, 19
Neuman, W F , Weikel, J H jun (1954) The Recrystallizatio Bone Mineral University of Rochester Atomic Energy Pro
Nicolaysen R Eeg Larsen, N Malm, O J (1953) *Physiol* **33** 424
*Nordin, B E C Roper, A (1955) *Lancet,* i, 431
*Owen E C Irving, J T , Lyall, A (1940) *Acta med scand* **103**,
*Pañella-Casas M. Montoya Orta (1950) *Rev med Liége* **5**,
*Plummer W A. Dunlap H F , Moore A B (1928) *Proc.* *Clin* **3** 119
*Polishuk Z Kleinhause E M (1952) *Gynæcologia* **133**, 1
Poumeau Delille G Fabiani J (1944) *C R Soc Biol* **138** 238
*Ravault P P , Graber Duvernay, J Léger, G (1939) *J med* **20** 69
Reifenstein E C jun , Albright F (1944) *New Engl J* **231**, 343
— — (1947) *J clin Invest* **26** 24
Riddle O (1942) *Endocrinology* **31**, 498
— McDonald, M. R (1945) *Ibid* **36**, 48
— Rauch, V M Smith G C (1944) *Anat Rec* **90**, 295
— Reinhart W H (1926) *Amer J Physiol* **76**, 660

Robinson, R. A (1952) *J Bone Jt Surg* 34A, 389
Rutishauser E., Dufour, J J (1950) *Schweiz. Z allg Path.* 13 781
Schoene R. H (1952) *Ohio med J* 48 126
Scowen, E. F (1948) *Proc R Soc Med* 41 735
Sherman, M. (1948) *J Bone Jt Surg* 30A, 915
Sissons, H A. (1952) *Ibid* 34B, 275
Smith, E. E., McLean, F C (1938) *Endocrinology* 23 546
Snapper I (1952) *Med. Clin N Amer* 36 847
Stevenson F H (1952) *J Bone Jt Surg* 34B 269
Strickland, B (1954) *Proc. R Soc Med* 47 341
Sussman, M. L., Copleman, B (1942) *Radiology* 39 288
Sutro, C J Pomerantz, L (1942) *Arch Path* 33 305
Teicher R. Nelson, C T (1952) *J invest Derm.* 19, 205
Thompson, D A W (1942) On Growth and Form. Cambridge
Vinther Paulsen, N (1953) *Geriatrics* 8 76
Vost, J H (1949) *Acta med. scand* 135 291
— Tanager A. (1949) *Ibid*, pp 231, 245
Ward, F O (1838) Outlines of Human Osteology. London
Weinmann, J P (1950) *In* Progress in Clinical Endocrinology Edited by S. Soskin New York.
— Sicher H (1947) Bone and Bones. Fundamentals of Bone Biology London
West E. F (1954) *Med. J Aust* 1, 84
Williams, R. H., Morgan H J (1940) *New int Clin* 2 40
Willis, R. A. (1936) *Proc roy Soc* B 120, 496
Wyse D M. Pattee C J (1954) *Amer J Med* 17 645

HIATUS HERNIA

SURGICAL RELIEF OF REFLUX ŒSOPHAGITIS

CHARLES WELLS
M.B Lpool F.R C S
PROFESSOR OF SURGERY UNIVERSITY OF LIVERPOOL

J H. JOHNSTON
M.B Belf F R C.S F.R.C.S.I
SENIOR SURGICAL REGISTRAR, LIVERPOOL ROYAL INFIRMARY

HIATUS hernia of the sliding type is a very common condition in which the tissues at the œsophageal hiatus of the diaphragm have relaxed and allow the cardio œsophageal junction to become retracted into the chest This retraction unfolds the acute angle between the œsophagus and the fundus of the stomach which normally prevents reflux of the gastric contents into the œsophagus (fig 1*a*) The hernial sac may occasionally be quite large but usually it is very small—indeed scarcely more than a potential sac which can be invaginated with the finger for an inch or so (fig 1*b*) The characteristic symptoms are caused by reflux and their severity does not depend on the size of the hernia

Ætiology

The ætiology is not fully understood, but advancing years obesity and increased intra abdominal pressure as in pregnancy all play a part Since the pressure within the abdomen is positive and the pressure in the chest negative it is perhaps not surprising that this hernia should appear from time to time, and its more frequent recognition in recent years may be related to dietetic and weight changes in the population Gall-stones are often found in association with hiatus hernia and may arise from common causes Hyperchlorhydria with duodenal ulceration is also a common concomitant and it is possible that in both cholelithiasis and ulcer a vagal reflex may cause muscular contractions of the œsophagus and so lead to retraction of the cardia More probably, however in duodenal ulcer it is the hyperchlorhydria which aggravates the effects of associated but unrelated reflux

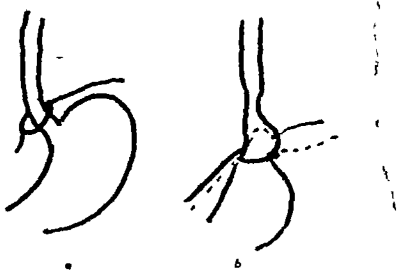


Fig 1—*a* Normal angle between œsophagus and stomach tends to *obstruct gastro-œsophageal reflux*; *b* *retraction* of cardia into thorax is followed by small sac of peritoneum (unfolding of cardia facilitates gastro-œsophageal reflux)

Symptoms and Diagnosis

The symptoms which suggest retracted cardia are heartburn (retrosternal burning pain) and acid regurgitation into the throat especially on lying down or on stooping Later there may be painful dysphagia from œsophagitis or ulceration or obstructive dysphagia from spasm or stricture The stricture may be annular from the healing of superficial lesions or may be due to dense fibrosis of the œsophagus and peri œsophageal structures causing organic fixed shortening Secondary anæmia from steady slight bleeding is not uncommon, and sharp hæmorrhage may rarely occur One of our patients had a fatal hæmorrhage from perforation into the aorta, and in another who recovered, a peri œsophageal abscess was caused by a penetrating ulcer These severe complications are quite unusual and are more likely to arise from ulceration at the level of *the hiatus* in the *gastric* pouch of a large hernia than from the commoner inflammation or ulceration of the œsophagus itself caused by reflux. The pain of a penetrating ulcer is experienced at the level of the lower ribs, especially *towards* the back. It may be excited by swallowing

Investigations to confirm and assess the condition comprise radiography a search for occult blood, the estimation of gastric acidity the *exclusion of* other disorders (e.g duodenal ulcer and gall-stones) and œsophagoscopy The endoscopy may reveal superficial ulceration spasm or stricture formation, redness and œdema or simply an abnormal *regurgitation* of gastric

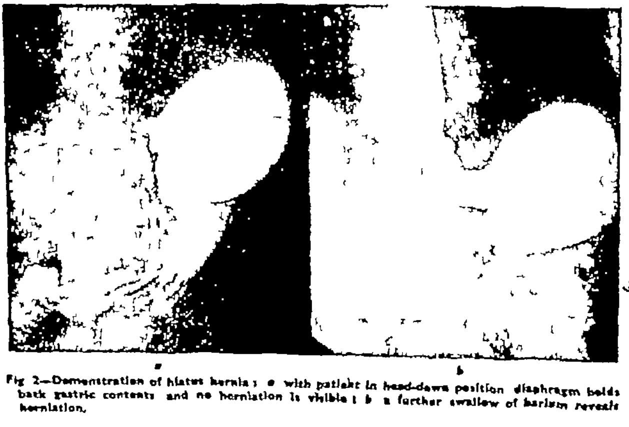


Fig 2—Demonstration of hiatus hernia; *a* with patient in head-down position diaphragm holds back gastric contents and no herniation is visible; *b* a further swallow of barium *reveals* herniation.

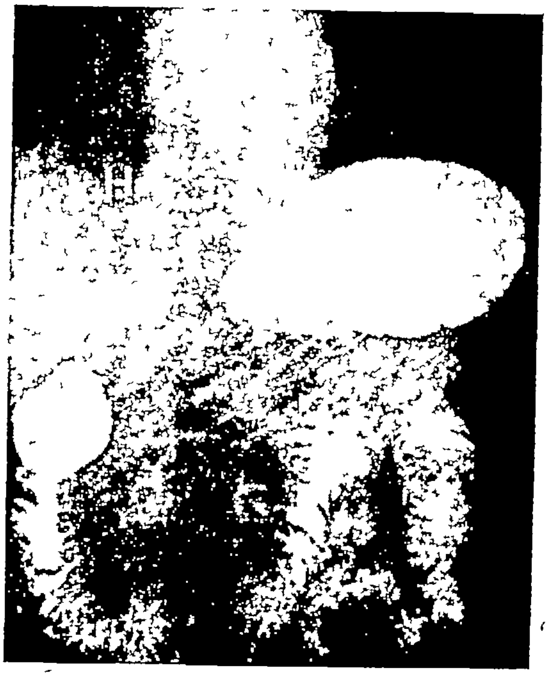


Fig 3—Typical small hiatus hernia.

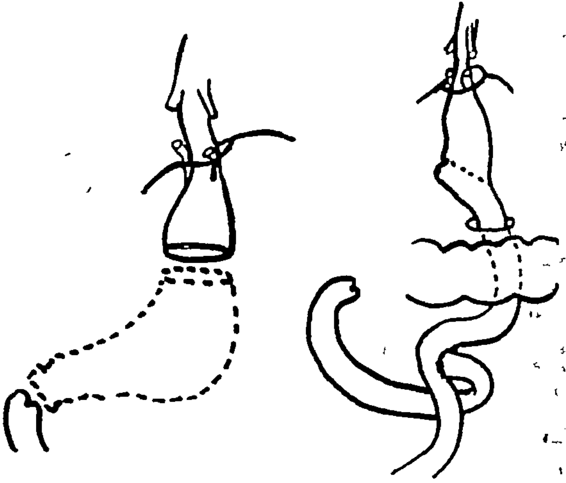


Fig 4—Scheme of operation described in text.

contents Gastric mucosa is seen sooner than is normal in some cases but not in all, since the instrument will displace the cardia downwards in the early and fully mobile case

A normal bismuth series may show retraction and incompetence of the cardia, or this may be demonstrable only with a special technique in which, after the meal, the patient, having been put in the head down position to show the fundus, is given a further bolus to swallow (fig 2) Even with the greatest care it may be difficult to distinguish with certainty between a small hiatus hernia (fig 3) and the physiological intermittent dilatation of the œsophagus, known as an epiphrenic ampulla, which is not associated with regurgitation Observation under the X-ray screen is of the greatest value and most instructive

Treatment

Non operative treatment gives a variable amount of relief Weight should be reduced, and food should not be taken for some hours before retiring, when antacids should be given as a nightcap The patient should be instructed to sleep propped well up with several pillows

Surgical Treatment — Conventional surgical treatment for those who do not get relief from non-operative measures is ordinarily directed to correction of the deformity By a thoracic approach the lower end of the œsophagus is drawn down to below the diaphragm and fixed there with sutures Reconstitution of the normal œsophago gastric angle is the essential and effective step Unfortunately most workers report a high incidence of recurrence after this operation, and in our own hands the recurrence rate has been so high that we no longer use this method

An alternative operation which we practise and advocate is based on a different principle We accept the incompetent cardia but seek to prevent regurgitation by securing rapid emptying of the stomach We also produce achlorhydria and divert the bile and pancreatic stream so that such regurgitation as may persist does no harm These desiderata are achieved by vagotomy, partial gastrectomy, and re anastomosis by the Roux method (fig 4) The approach is from the abdomen

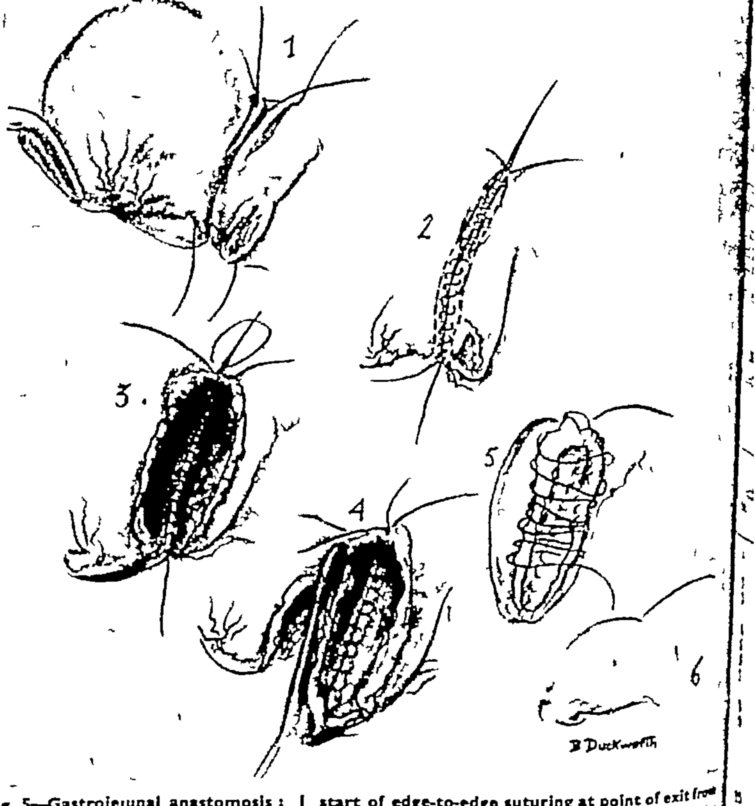


Fig 5—Gastrojejunal anastomosis : 1 start of edge-to-edge suturing at point of exit from stoma near greater curve 2 continuation of this suture line as conventional seromuscular suture and indication, by interrupted lines, of incisions into stomach and jejunum 3 posterior suture line completed and corner at open end of jejunum trimmed away; 4 distal part of stomach being cut away , 5 anterior suture line taking mucosa alone near greater curve and all coats elsewhere (cf fig 6) 6 suture-line completed

und consequently enables any associated abnormality o be given appropriate attention

The diagnosis is confirmed by palpation of the hiatus, hrough which a pouch of peritoneum can be palpated or expelled by the examining finger If the hernia can still be educed which is usual, the left lobe of the liver is mobilised he peritoneum incised around the hiatus, and the oesophagus freed and drawn down into the abdomen for an inch or two Vagotomy is then carried out in the usual way If a completely satisfactory denervation is not achieved this fact should be carefully noted, so that in the event of pain recurring a transthoracic vagotomy may be advised If the patient is obese or if the oesophagus cannot be pulled down, vagotomy by the transthoracic approach becomes obligatory

The gastrectomy follows the usual lines. We like to conserve the gastro-epiploic arch. In hiatus hernia we do not always divide the left gastric vessel near its origin; alternatively we divide the descending branch on the lesser curve About two-thirds of the stomach is removed, and the duodenum is carefully closed as usual.

The upper jejunum is then displayed and a point is selected a few inches beyond the flexure for its division Nutrient vessels are sacrificed and arcades preserved in such a way that the jejunum distal to the cut can be drawn up through the mesocolon and anastomosed to the stump of the stomach without tension The opening at the cut end of the jejunum is extended by an incision along its antimesenteric border and the resultant corners are trimmed away The anastomosis is made with great care at the point of exit at the greater curve since easy emptying of the stomach remnant is essential to success. Sometimes at this point in the anastomosis we use the edge-to-edge technique illustrated in fig 6 The mesocolon is finally fixed to the stomach proximal to and around the stoma.

The anastomosis in Y is completed about twelve inches below the stoma by bringing the biliary loop underneath and round to the left side of the vertical limb To avoid any narrowing of the jejunum carrying the food-stream (the vertical limb) the suturing is done with meticulous care in a special manner As illustrated (fig 6) the seromuscular coats are joined edge to edge with a continuous catgut stitch the loops of which are placed as delicately and as close together as possible The posterior mucosal layer is oversewn, and the stitches almost encroach on the first layer The anterior mucosal layer is made with a Connell stitch almost encroaching on the cut seromuscular coats, and these are finally sutured together as in the first layer This close suturing controls haemorrhage whilst the use of the extreme edges of the structures avoids constriction in a remarkable way

During the anastomosis it is impossible to control bleeding from the jejunal ends with the ordinary bowel clamps, but we have found that Crile's vessel-clamps on the mesenteries are excellent.

Discussion

It is twenty years since one of us performed his first gastrectomy for hiatus hernia. There was a large fixed hernia with a penetrating ulcer of the stomach at the level of the hiatus Polya gastrectomy below the level of the ulcer (Wells 1933) was undertaken as a first-stage procedure It gave complete relief and no further treatment was required More recently however, we have been disappointed with the results of both the Polya gastrectomy and the Steinberg (1940) modification in the presence of retracted cardia because of the persistent

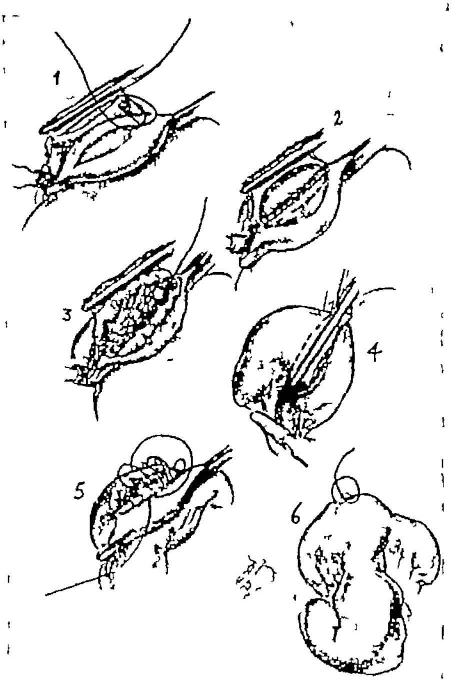


Fig 6—End-to-side jejunal anastomosis by edge-to-edge technique; 1 seromuscular coats joined; 2, incision through mucosa indicated; 3 posterior mucosal layer completed; 4 final seromuscular incision at end of afferent loop indicated; 5 anterior mucosal closure with Connell's stitch; 6 edge-to-edge seromuscular suture completed.

HIATUS HERNIA FORMER OPERATIONS, ASSOCIATED DISORDERS, AND PRESENT SYMPTOMS

Patient no.	Sex	Age (yr)	Former operations	Associated abdominal disorders	Duration of follow up (mos)	Present symptoms	Weight
1	F	56	None	None	14	Sensation of fullness after meals	Gain
2	M	50	None	Duodenal ulcer	13	Eupeptic	Loss
3	F	63	None	Duodenal ulcer cholelithiasis, cholecystectomy done	13	Eupeptic	Slight loss
4	M	57	None	Duodenal ulcer	12	Eupeptic	Unchanged
5	M	28	None	None	10	Eupeptic	Gain of 1 st.
6	M	74	None	None	10	Eupeptic	Unchanged
7	F	61	None	None	4	Sensation of fullness after meals	Unchanged
8	M	49	None	None	4	Eupeptic	Unchanged
9	F	40	Heller's operation 1950 transthoracic repair of hiatus hernia 1951 Steinberg gastrectomy for recurrent hernia 1952	None	4	Eupeptic	Slight gain
10	F	45	Steinberg gastrectomy 1953	None	2	Palpitations after meals, occasional regurgitation of clear fluid	Unchanged
11	F	30	None	Cholelithiasis cholecystectomy done	2	Eupeptic	Unchanged
12	F	61	Cholecystectomy 1940	None	[illegible]	Eupeptic	Unchanged

vomiting of bile In patients 9 and 10, who had each undergone Steinberg gastrectomy, the symptoms of œsophagitis persisted, and there was profuse regurgitation of bile on recumbency or stooping Conversion of the anastomosis to the Roux type, without disturbing the original gastrojejunal stoma, and vagotomy, have produced, in patient 9, complete relief of dyspepsia and gain in weight Patient 10 had also complained of palpitations after food, following the gastrectomy This symptom has persisted to a lesser degree after the conversion operation and, in addition, the patient has occasional reflux of clear fluid into the mouth

The cases are summarised in the accompanying table The predominant complaints in the three patients with concomitant duodenal ulcer were related to the incompetent cardia rather than the ulcer The history of the remainder conformed to a common type, and the following is *typical*

Case 6—A man, aged 74, was admitted to the Liverpool Royal Infirmary in August, 1953, with four years' history of burning epigastric and retrosternal pain radiating to the neck and regurgitation of acid fluid into the mouth on lying down He was often wakened at night by a choking sensation due to fluid in the throat, and there were pain and difficulty in swallowing and loss of weight Probable œsophageal carcinoma had been diagnosed in another hospital

On admission clinical examination was negative Radiography showed slight spasm in the lower œsophagus and, in the Trendelenburg position, revealed a sliding hiatus hernia with incompetence of the cardia A fractional test meal showed hyperchlorhydria Retraction of the cardia and œsophagitis were confirmed at œsophagoscopy, but, in view of the patient's age, medical treatment with diet, alkalis, and an inclined sleeping posture was advised

Progress—Seven months later the patient was readmitted with no improvement in his symptoms and requested an operation Ten months after operation he is free from dyspepsia and has returned to his work as a hairdresser

All our patients obtained complete relief from their main symptoms by operation Subsequent fractional test-meal or 'Diagnex' tests have shown achlorhydria, which suggests that vagotomy and two-thirds gastrectomy do in fact protect the Roux anastomosis from the danger of stomal and jejunal ulceration which formerly led to its abandonment in the treatment of peptic ulcer In case 8, because of difficulty in exposure, vagotomy was not performed with the gastrectomy The patient remained well until three months later, when there was a recurrence of heartburn and pain on swallowing, which was relieved by alkalis Eupepsia has been restored by transthoracic vagotomy

It was feared that the entrance of bile and pancreatic juices into the alimentary tract at a distance from the stomach might interfere with normal digestion and absorption and lead to a deficiency type of post gastrectomy syndrome, but some of the patients have in fact gained weight and in none has there been a significant loss There has been no evidence of vitamin deficiency It is too soon to be sure whether or not microcytic iron-deficiency anæmia will develop, but it is, if necessary, easily corrected (Wells and Welbourn 1951)

Summary and Conclusions

Attention is drawn to the frequency of retracted cardia and gastro œsophageal reflux as a cause of dyspepsia

The diagnosis of the condition is outlined and, for its treatment, an operation which is new in this context is described It consists in vagotomy, partial gastrectomy, and re-anastomosis by the Roux-Y method

Satisfactory early results in twelve consecutive cases are summarised

REFERENCES

Steinberg, M E (1949) *Surg Gynec Obstet* 88 453
Wells, C A (1933) *Brit med J* i 778
— Welbourn, R B (1951) *Ibid*, i, 546

THE MANAGEMENT OF CHILDREN UNDERGOING TONSILLECTOMY

PREMEDICATION WITH METHYLPENTYNOL

F R GUSTERSON
B Sc, M B Lond, F.F.A R C S
ANÆSTHETIST, WORTHING GROUP OF HOSPITALS, SUSSEX

It is estimated that every week, in Great Britain alone 1500 children undergo tonsillectomy In most cases this will be their first experience of hospital, and the responsibility for seeing that it does not cause emotional harm which may affect the child's whole life, rests largely on the anæsthetist Though much has already been written on the subject[6 14 16 17 20] *it is one which should be continually reviewed in the light of new methods*

Admission to Hospital

With a child of under 5 years of age, the important question is whether he has already learnt to adjust to separation from his mother by the normal process going to school If this has not yet happened, no amount of sedation with drugs will save him from being mentally hurt by this forced separation So important did the late Sir James Spence feel this to be that he devot much of his energies to establishing a hospital unit which mothers had to remain in hospital with th *babies It would be difficult to insist on this for* tonsil cases, but much can be done even in routi hospital work to minimise the emotional trauma

So far as is practicable, each block of admissions sho be of a similar age group The constant crying of 2-year-old can be very upsetting to a 10 year-old, in addition the older boy resents being in hosp "with kids"

The mothers of all children of age groups usu admitted to children's wards should not only bring child into hospital but should give him his first bath put on his night-clothes, which could, with advant be the child's own Many children feel more secure their own clothes The time of admission is import and should never be *in the morning unless* th absolutely unavoidable To put a young child to in the morning is synonymous with punishment first meal in hospital should be given by the mot aided by the nurse who will look after the child. raises a very important point The number of pe dealing with the child should be as small as possib ideally one nurse only, *who will thus become* temporary mother substitute

While the mother is still present, the child sho meet as many as possible of the people whom he will next day, including theatre porters All these pers should be chosen for their ability to handle childre there is a type of hospital porter who would frighten child out of its wits *If not already done at home,* would be a *good time to tell the child* exactly what happen the following day

One point which should be emphasised is the imp tance of the child's bringing into hospital some favou toy, however shabby This is brought out very well Robertson's[28] film, in which the toy is a piece of well chewed *blanket* The toy will be *returned* the child, *for the old idea of infection* being transmit *in* this way is no longer held This toy will natur accompany the child to the operating theatre, which the end of a morning's list may thus look rather lik scene from a Walt Disney cartoon The toy must be in the cot when the child wakes up

On the Way to the Operating-theatre

If the child is not asleep when his time comes to to the theatre he should never be made to lie down the trolley *To lie flat on the back while being wh* along corridors is very *frightening* The operat hould be carefully timed even when this means some nconvenience All operations on children should be done as early as possible in the day A child will tolerate the absence of his breakfast, but the absence of dinner s well, particularly if other children in the ward are having theirs, is really putting too great a strain on his control

Two more simple points are worthy of mention here The first is the old fashioned practice of making the child wear a mackintosh cap and bib for tonsillectomy With modern surgical techniques this surely is no longer necessary, and the children are much happier without them.

The other point is the wearing of face masks by the theatre staff It is most important that every person handling a child on his way to the theatre and in the anæsthetic room should have the face fully exposed Half masked faces are extremely frightening to children and it is a great help to the child to be able to recognise his ward nurse

Sedation

Many anæsthetists feel that to avoid any possible emotional upset all children of whatever age should be completely asleep before leaving the ward for the theatre This would in many ways be ideal provided that the perfect drug or combination of drugs could be found ven so the remarks in the foregoing paragraphs still pply to the time before and after the child has its actual eration and I suggest that however perfect the asleep in the ward ' technique is some case will occur here sedation is incomplete Many think although it difficult to prove that in the resulting partially dis ientated state a child is even more impressionable than hen fully conscious This certainly applies to adults many will remember from the early days of the use barbiturates by mouth for premedication

Innumerable methods have already been used to nsure that every child is fully asleep before leaving the ard, and each has its enthusiastic advocates Having ied them all I have given them up one by one Person ly, I feel that the rectal administration of drugs to ildren should be avoided except when absolutely ecessary Children may not like an injection or a nasty edicine but that is an affair of the moment that a ild can have explained to it. Not so with rectal terference, and the very young child is also psycho gically sensitive about its rectum Hence while mitting the safety of rectal paraldehyde and the noothness of rectal thiopentone I cannot agree that ey should be used as a routine practice Furthermore did find when using rectal paraldehyde in children some ears ago that many had postoperative pyrexia and for everal days were not fit to return home The dis dvantages of any barbiturate (see below) are also pplicable to rectal thiopentone

I have also used morphine for premedication either as orphine and atropine or as Omnopon and hyoscine, sing the dosage schedules advocated by various orkers[3,16] I was immediately confronted with an crease in postoperative vomiting and complaints from he ward sister that quite a number of children were angerously depressed on return to the ward, and that reat difficulty was experienced in keeping their airways lear The dosage of these extremely potent drugs is mall and minute errors can have serious consequences

At present the drugs most popular for premedication re pentobarbitone ('Nembutal') and quinalbarbitone 'Seconal') Though undoubtedly satisfactory in many ases these have very grave disadvantages I have ound very little to choose between them and I wonder hether it would be possible to differentiate between hese two drugs by purely clinical assessment The ollowing remarks about pentobarbitone therefore apply qually to quinalbarbitone

Barbiturates

In the first paper on pentobarbitone in this country Magill[31] wrote

> ' As with other barbiturates the variable reaction of individuals to nembutal renders the dosage by mouth and by rectum difficult to determine beforehand This is especially noticeable in children. In general, it may be stated that children are more resistant than adults and in children the variation has little to do with age or development For example, one well-developed child age 7 was fast asleep after the administration of grs. $1^{1}/_{4}$, while another child aged 6 and of small physique was quiescent but not asleep after grs. 3 had been given.
>
> He further said that ' Irrespective of the dose or method of administration, a variable degree of restlessness was noted during the immediate post-operative period in 13 patients Five were children and their condition was controlled by potassium bromide

Waddy[30] confirmed the postoperative restlessness and in subsequent articles on these drugs the same two drawbacks of uncertainty of effect and postoperative restlessness have been mentioned[4,6,12,18,22] This still applies, even if in a lesser degree, when the drug is given rectally

Postoperative restlessness is a more serious problem than this uncertainty of dosage, and can be so great that a single nurse can hardly control the child A wardful of such children is in a real state of pandemonium, which can be reduced to a manageable degree only by giving morphine or one of its derivatives.

From the state of uncontrolled restlessness it is so easy to pass to that of an uncontrolled airway serious enough after any operation but liable to be extremely dangerous *after an operation* on tonsils and adenoids By whichever method the operation is done, blood is apt to accumulate in the upper respiratory passages Again even if the airway is not obstructed there is the very real risk that blood and mucus will be inhaled into the lungs during the state of respiratory depression which may follow the giving of morphine after a barbiturate

I was delighted to see attention drawn to this by Fraser[9] and Middleton Price[24] The situation is often made worse by ordering further morphine to control the hæmorrhage I recently had experience of such a case and at necropsy the lungs were full of inhaled blood which had without doubt been the cause *of death I have indirect knowledge of other* such cases which could usefully be made known and discussed Even if this complication occurs only in 1 case in 2000 it is too high a price to pay for the doubtful advantage of the child's being asleep before leaving the ward.

A much less important difficulty with these barbiturate preparations is that of administration They all have an extremely unpleasant and long lasting taste and hence are supplied in capsules Nurses have developed many ingenious ways of administering these but often several mouthfuls of water are given When there has been some emotional upset during the attempt to swallow the capsules this may not be absorbed from the stomach, with the result that the child vomits during the induction of anæsthesia Also in such cases the drug has not usually been absorbed and the child is still awake, thereby losing the whole purpose of this method. The drug may become absorbed later, another factor contributing to postoperative respiratory depression With these draw*backs in mind I had* for some time relied on atropine alone for premedication induction usually being by intravenous thiopentone—a technique used by many others But in spite of the most careful handling about 20% of the children were obviously much upset by the visit to the theatre and yet another injection

Methylpentynol

The advent of methylpentynol therefore seemed to offer a via media between the dangers of a barbiturate and the disadvantages of no preoperative sedation All the early reports[2 7 10 11 13 22 23 25 26] of its use as a hypnotic emphasise the absence of side effects, especially respiratory depression and alteration of blood-pressure or pulse Methylpentynol was reported as having a specific effect in allaying fear and apprehension, even in doses where actual sleep was not obtained It is available commercially as a flavoured coloured elixir of ‘Oblivon’ (British Schering) containing 250 mg of methylpentynol per teaspoonful The flavour cannot be described as pleasant—it vaguely suggests paraldehyde—but in actual practice children very rarely complain about it

As soon as this investigation was planned, it became necessary to find some method of recording the children's reactions which would be impersonal and in no way subject to bias or prejudice It was decided to follow the work of Robertson of the Tavistock Clinic and make a film record showing children's reactions with different forms of premedication Cases were chosen at random by the camera operator from routine operating-lists This film is now available and demonstrates better than words the reactions of the children In nearly every case the child looks happy not only on going up to the theatre but also—perhaps more important still—on waking up in the ward afterwards

We soon found that in many cases the doses recommended by the makers had little effect We now give two teaspoonfuls for children aged 2–4 years, three teaspoonfuls for children of 4–8 (varying slightly with the build or temperament of the child), and four teaspoonfuls for children of 8–10 The methylpentynol should be given an hour before the anæsthetic, and the atropine can then be given half an hour later, when the child is much less upset by having an injection With these larger doses the children nearly all arrived in the anæsthetic room quiet and apparently unperturbed, some actually asleep though easily aroused Brown and Ellis[5] confirm the great safety margin of methylpentynol

In nearly every case anæsthesia was induced with a “sleep dose” of intravenous thiopentone This is a safe and easy procedure in a quiet and peaceful child, but the possibility of an intra-arterial injection has always to be borne in mind Attention was first drawn to this by Macintosh and Heyworth,[19] but there should be no difficulty in these cases, because the child will cry at once if the artery is touched If the child cries at all, the position of the needle must be checked, and, if there is any doubt, the injection is not continued Instead it is quite easy to induce anæsthesia with nitrous oxide without distress to the child

With this method no difficulty from vomiting in induction (Rendell[27]) has been observed, nor has there been any increase in postoperative vomiting I think the difference in my series (which now extends to more than 500 cases) is due to the fact that the methyl pentynol has been given early enough to be absorbed from the stomach

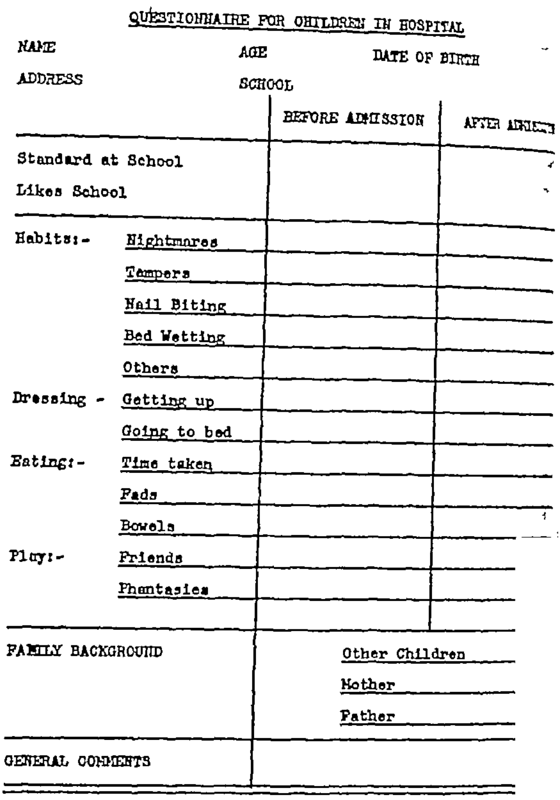
The ward immediately commented on the greatly decreased degree of postoperative restlessness in children premedicated with methylpentynol Children given no postoperative ‘Nepenthe’ were carefully watched and showed little restlessness, what little there was ceased in a few minutes No special control was required Absence of respiratory depression was quite obvious, and the children could keep their own airways clear even if they rolled over on to their backs This was equally true after an injection of nepenthe minim 1 per year of age With such a dose the children all remained peacefully asleep, and it is now our routine to give this injection as soon as the child shows signs of returning to consciousness

Before deciding on the value of this new method of preoperative sedation it was necessary to study it from the child's point of view A survey of these children was therefore undertaken along the lines o Albany Research Project[1] An experienced psych social worker was employed who also had a know of general hospital routine and an understandi children She was given the admission lists fro record department of the hospital and chose 100 ca random I did not know which cases she had visite she did not know what anæsthetic technique had used in any particular case Thus any possible b opinion was eliminated. The children chosen visited in their homes about a week before admissio again several days after their return home Many of children were visited several times in a period up to weeks after their discharge from hospital

Several interesting factors emerged from this in gation The first was the great advantage of a “by somebody from the hospital” The child's m and the child had the whole episode explained in s non-technical language It would be an excellent w reducing fear of hospital if this could be done in e case, if not, perhaps a simple letter explaining routine in hospital could be sent with the admi note

The questionnaire is shown in the accompan figure This is quite a simple form because it was considered advisable to make each child into a psy logical study, but all the necessary facts are incl in it

The numbers of children receiving pentobarbitone methylpentynol were almost equal This was q fortuitous At once it was evident that the propor of children disliking their hospital experience was eq in each case (see table)



QUESTIONNAIRE FOR CHILDREN IN HOSPITAL

NAME AGE DATE OF BIRTH
ADDRESS SCHOOL

		BEFORE ADMISSION	AFTER ADMI
Standard at School			
Likes School			
Habits:-	Nightmares		
	Tempers		
	Nail Biting		
	Bed Wetting		
	Others		
Dressing -	Getting up		
	Going to bed		
Eating:-	Time taken		
	Fads		
	Bowels		
Play:-	Friends		
	Phantasies		

FAMILY BACKGROUND
Other Children
Mother
Father

GENERAL COMMENTS

REACTION TO STAY IN HOSPITAL

—	Received pentobarbitone	Received methylpenty
No of children	51	49
Reaction favourable	40	39
Reaction unfavourable	11	10

'he "unfavourable reactors" varied in their com laints Most mentioned specifically a dislike of pricks," while others merely mentioned that they did ot like having to sleep in a room with the lights on or hat they did not like the food

The number of children showing any real emotional pset was quite small in each series. Of those receiving entobarbitone 3 showed increase of nightmares and of hose receiving methylpentynol 5 showed emotional upset uch as crying at night, and disinclination to return to chool Children showing this emotional upset were all nder 6 years old

It is therefore fair to deduce from this admittedly mall survey that there is no specific advantage from the hild's point of view in heavy preoperative sedation that btained with methylpentynol being adequate to prevent any appreciable psychological trauma

The number of children mentioning an objection to the njection was considerable, and equal in each series This ed me to think of some method of avoiding the injection of atropine At first the atropine was dissolved in a ittle water in doses of gr $^{1}/_{100}$–$^{1}/_{50}$ according to age, nd this solution was added to the elixir This had a efinitely adverse effect on the not too pleasant taste of he elixir and in addition the children were not dry nough for comfort during induction or operation At he same time it was thought that the sedation obtained as not so good, but since secretions were not adequately controlled, only a few cases were investigated

Hyoscine was next used in the same way in doses of $^{1}/_{150}$–$^{1}/_{75}$ This did not affect the taste of the xir and in every case the drying effect was satis tory In addition there was a much greater sedative ect. Nearly every child arrived in the anæsthetic om actually asleep, although easily aroused. In the stoperative stage there was no restlessness and even nepenthe was given the children were quite easily oused. The ward nurses in fact commented that the ildren seemed to sleep naturally for the rest of the day ter returning to the ward although they could be used quite easily and given a drink after which they ietly settled down and returned to sleep This modifi tion has not yet been used in many cases but so far ows great promise

It thus seems that methylpentynol, given as elixir of ethylpentynol provides a safe and reliable premedica on for children There is no increase in emotional set even if the children are not actually asleep on rival in the anæsthetic room Induction of anæsthesia ith a sleep dose of intravenous thiopentone gives a very nooth and pleasant induction and there is no danger of stoperative respiratory depression The addition of yoscine to the methylpentynol by mouth thereby voiding two injections, is at the moment being investi ated and shows every prospect of being successful

Summary

It is important to avoid emotional trauma in children dmitted to hospital for tonsillectomy especially when ey are under 5 years of age

Simple points in the management of children during eir stay in hospital are outlined

The disadvantages and dangers of using barbiturates r preoperative sedation are discussed

The use of methylpentynol in a flavoured elixir for eoperative sedation is described A follow up of 100 ses showed no difference between the emotional response f those children sedated with pentobarbitone and those ceiving methylpentynol Methylpentynol has a great fety margin and none of the disadvantages of the rbiturates

A sound film has been made illustrating the points the paper

I am indebted to Mr H G Downer and Mr P C Rushton hose cases these were and who performed all the operations I wish to acknowledge the very great help and coöperation I have received from the nurses of the E N T wards of Worthing Hospital. The children were visited by Mrs. E E Nevell, some time psychiatric social worker attached to Graylingwell Hospital The expenses of this investigation and of making the film were met by a grant from the research funds of the South West Metropolitan Regional Hospital Board. The photography was under the charge of Mr J Howard Dr R Mac Keith helped with the script of the film

REFERENCES

1 Albany Research Project (1952) Reducing Emotional Trauma in Hospitalized Children New York.
2 Allen, A W., Krongold D D (1951) *Quart Bull Sea View Hosp* 12 61
3 Anderson, S M. (1951) *Lancet* ii 965
4 Boston F K., James, N R. (1941) *Brit med J* i 5
5 Brown, I M., Ellis R A (1955) *Ibid* i 268
6 Bullough J (1952) *Lancet* ii, 999
7 Chevalley, J Hemingway, N Moyer G., Frankhauser R McGavack T H (1952) *N Y St J Med* 52, 542
8. Eckenhoff J E (1953) *Amer J Dis Child* 86, 587
9 Fraser G A (1954) *Proc R Soc Med* 47 954
10 Gangemi, C R (1952) *Int Rec Med* 165 109
11 Giaidroni, C. Grassi O (1952) *Atti Soc lombarda Sci. Med Biol* 7 90
12 Gorham, A P (1935) *Brit med. J* ii 112
13 Hirsh H L. Orsinger W H (1952) *Amer Pract Dig Treatm* 3 23
14 Jackson, K. (1951) *Anesthesiology* 12 293
15 — Winkley R. Faust O A., Cermak, E. G (1952) *J Amer med Ass* 149 1536
16 Leigh, M. D Belton, M K (1946) *Anesthesiology* 7 611
17 Levy D M. (1945) *Amer J Dis. Child* 69 7
18 Lorber J (1950) *Brit med J* ii 21
19 Macintosh, R. R., Heyworth, P S. A. (1943) *Lancet* ii 571
20 Mac Keith, R. (1953) *Ibid*, ii, 843
21 Magill, I W (1931) *Ibid* i 74
22 Malone H J., Klimkiewicz, G R. Gribetz, H J (1952) *J Pediat* 41 153
23 Margolin, S. Perlman P L. Villani F J., McGavack, T H (1951) *Science* 114 384
24 Middleton Price J (1954) *Proc R Soc Med* 47 954
25 Moravec C. L., Moravec M E (195[illegible]) *Med Times, N Y* 80 301
26 Papa, D Villani F J Ginsberg H F (1951) *Arch. Biochem Biophys* 33, 482
27 Rendell C M. (1954) *Brit med J* i 641 *Ibid* ii 1397
28. Robertson, J (1952) A Two year-old Goes to Hospital (film) Tavistock Clinic.
29 Royal Society of Medicine (1940) *Proc R Soc Med.* 33 [illegible]83
30 Waddy F F (1933) *Brit. med J* ii 234

CHEMICALLY IDENTIFIABLE BACTERIAL RESIDUES IN LUNG LESIONS

R Consden
Ph.D Lond. A.R.I C
RESEARCH BIOCHEMIST
L E Glynn
M.D B Sc Lond. M.R C P
DIRECTOR OF THE DEPARTMENT OF PATHOLOGY
THE CANADIAN RED CROSS MEMORIAL HOSPITAL, TAPLOW, MAIDENHEAD, BERKS

The syndrome described by Caplan (1953) in coal miners with pneumoconiosis consists in the development of radiologically characteristic pulmonary nodules in patients with concomitant rheumatoid arthritis In a community of South Wales coalminers Miall, Caplan Cochrane Kilpatrick and Oldham (1953) found that more than half the men with this characteristic X ray picture also had rheumatoid arthritis compared with only 3% of those with ordinary progressive massive fibrosis

Because of our work on the chemistry of the subcutaneous nodules of rheumatic fever (Consden Glynn and Stanier 1953) we were invited by the South Wales investigators to study the chemistry of these various lung lesions with a view to confirming the difference between the Caplan nodule and other forms of pneumoconiotic fibrosis In the course of this work we found that in some samples the hydrolysates appeared to contain α ε diaminopimelic acid (D A P) when examined by paper chromatography Since this amino acid is not a normal constituent of mammalian tissue but is widely distributed among bacteria of various genera and species including *Mycobacterium tuberculosis* it seemed important to establish with more certainty that D A P was present especially as infection was no longer demonstrable by the usual methods of microscopy, culture, and animal inoculation This method of detection is presented below

Tissues Studied

(1) *A caseous nodule* obtained by biopsy from a man aged 23 was a typical caseous tuberculoma 1 5–2 0 cm in diameter with an acellular non-fibrous necrotic centre surrounded by a zone of cellular fibrous tissue 2–3 mm thick Occasional foci of epithelioid and giant cells were present in this cellular zone No acid fast bacilli were found despite prolonged search of several sections

(2) *Tuberculous lung tissue* obtained by biopsy from a woman aged 28 contained several dense fibrous foci acellular in the centre and only slightly cellular at the periphery The apparently necrotic centre, when stained by Gomori's (1937) method for reticulin, revealed a dense network of fine and coarse collagen fibres with some still finer argyrophil fibrils interspersed with them No tissue histologically characteristic of tuberculosis was seen, and no acid fast bacilli were found

(3) *Progressive massive fibrosis* a sample removed at necropsy from a man aged 55 consisted of jet black and fairly dense fibrous tissue about 1 cm in diameter and surrounded by a narrow margin of emphysematous lung The main fibrous lesion consisted of a dense central network of collagen with a surrounding fibrous capsule radiating into the surrounding lung Similar but smaller nodules were present in the adjacent lung tissue The acellularity of the fibrous tissue was striking

(4) *Infective nodules* obtained at necropsy from a man aged 57 consisted of densely pigmented lung with diffuse fibrosis and some nodules up to 2 mm in diameter formed of interlacing collagen fibres. Cellular reaction was virtually absent from the fibrous areas and the intervening lung tissue

(5) *A Caplan nodule* obtained at biopsy from a man aged 52 was a sharply defined lesion about 1 5 cm in diameter Histologically the main central part of the nodule appeared structureless or faintly fibrillar when stained with hæmatoxylin and eosin, but with silver impregnation this central area was seen to be composed of a dense network of collagen fibres with finer argyrophil fibrils in the interstices Peripherally there was a band of cellular tissue containing fibroblasts and foci of lymphocytes and histiocytes, but the cells were not in a palisade formation The microscopic appearance lacked the characteristics of tuberculosis, and the structure of the acellular centre was quite different from that of the subcutaneous nodules of rheumatoid arthritis

(6) *Normal lung removed* at necropsy from a male town dweller, aged 59, who died of congestive cardiac failure consisted mainly of the dark dusty surface and was used as a control of the other lung specimens

Method of Demonstrating D A P in Lung Lesions

Samples of all the lung tissues were washed with 0 8% saline solution followed by distilled water, dehydrated in acetone, and autoclaved to remove collagen Tests for D A P as described below were made on the residues, since preliminary chromatography had indicated that in tissues which contained this amino acid, the bulk of it was not extracted by autoclaving This procedure therefore has the advantage of concentrating the D A P-containing constituents in the test material, because from a half to two-thirds of the organic material of the lung samples was removed by autoclaving The residues of Caplan nodule, tuberculous lesion, and progressive massive fibrosis after autoclaving contained about one-third of the original organic matter, whereas the infective nodule and caseous nodule residues contained about one-half

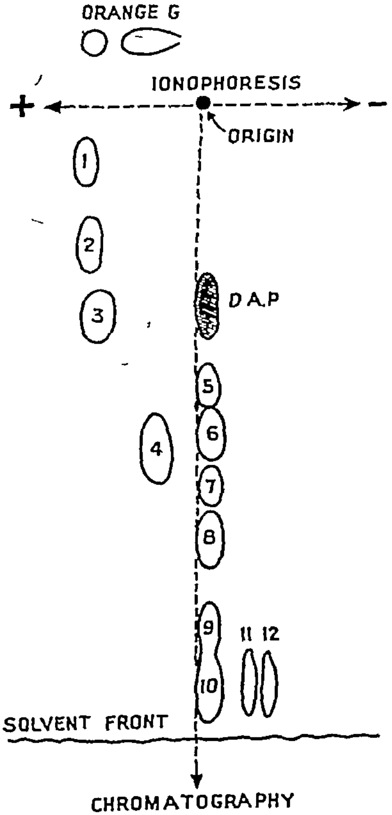
The following simple test for D A P depends on a two-dimensional separation on paper by chromatography followed by ionophoresis at right angles to the direction of chromatography

The tissue was hydrolysed with 6 N HCl at 105–110°C for 17 hours Excess acid was removed by evaporation in vacuo Insoluble humin was separated by centrifugation A portion of the hydrolysate was treated with excess bromine water and stood for 5 minutes Excess bromine and acid were removed by evacuation over KOH. The treated hydrolysate was concentrated to a suitable volume, and 5–10 µl containing the equivalent of 0 25–0 33 mg of protein was placed o spot half-way across a sheet of Whatman no 1 filter pa 24 cm wide Chromatography was carried out in wa saturated phenol in an atmosphere of NH_3 (produced fr 0 3% NH_3 on the floor of the chamber) for 21–24 hr., which time the solvent front had travelled about 25 c from the origin. The sheet was thoroughly dried and the pa below the solvent front removed The remainder was suspen and sprayed lightly and evenly with M/20 phosphate buff pH 7, the spraying being done first on either side of t chromatogram and finally along the chromatogram itse The wet sheet was then placed in position in the pap electrophoresis apparatus with the edges of the paper dipp into the electrode compartments containing M/20 phospha buffer, pH 7 The apparatus consisted of a flat shall 'Perspex' box designed for holding paper in a horizont position Before the current was applied, a drop of Orange solution was placed above the origin to act as a control. T voltage applied was about 14 V per cm, and the start current 0 5 mA per cm of width The current was pas for 1 hour, after which the paper was removed, dried, a treated in the usual way with ninhydrin During the io phoresis the Orange G separates into two components (r and yellow) The faster (yellow) travels at a similar rate aspartic acid and hence is useful for observing progress dur the run The resulting two dimensional separation (chroma phoretogram) is illustrated diagrammatically in the acco panying figure

In phenol NH_3 the amino acids which would interfere w D.A.P are glutamic acid, ethanolamine phosphoric acid, a cystine, all of which occur in animal tissues. The first t because of their acidic nature, migrate towards the an in an electric field Cystine is completely oxidised Br_2 to cysteic acid (Consden et al 1946), which bes having a lower R_F value than D.A.P, is also acidic D.A behaves li the monoami monocarbox acids and migra slowly towards cathode becaus electro endosmo and no kno amino acid of animal tiss hydrolysate wo occupy the s position after two dimensio separation Ty sine, if present converted by bromine to dib motyrosine, wh migrates slow towards the an at pH 7 and h an R_F value phenol similar glycine The ba amino-aci migrate towar the cathode

Work an Dewey (1953) de cribe a method demonstratin D.A.P, based similar princip but this is mo laborious an time consumi than the meth described abov

A number o solvents can b used for the f chromatograph separation bet the interfer components



Chromatophoretogram of a bromine-oxidised protein *hydrolysate containing* diaminopimelic acid (chromatography in phenol-NH_3 *followed by ionophoresis at pH 7*)

D.A.P, *diaminopimelic* acid 1 cysteic acid 2, aspartic acid 3 glutamic acid (ethanolamine/phosphoric acid if present, would *occur here*) 4, dibromotyrosine 5 serine 6, glycine 7 threonine 8 alanine 9 valine 10 leucine &c. 11 arginine 12, *lysine*.

be subsequently separated by ionophoresis or converted to acidic amino-acids by oxidation. However, solvents which incorporate acid are a disadvantage because it is impossible subsequently to remove all the acid from the paper. This increases the ionic strength of the buffer and hence causes too high a current for convenience in the ionophoretic separation. Further, if ethanolamine phosphoric acid were present it would only have appreciable ionophoretic mobility at pH 6 or higher (Clarke et al. 1955). The acid in the paper would therefore require stronger buffer solutions to raise the pH sufficiently, and this would also cause high current. This could be overcome by using a lower voltage, but the time of ionophoresis would be correspondingly increased. The width of the sheet is not important; it depends on the dimensions of the paper-electrophoresis apparatus used.

Results

The lower limit of detection of D.A.P. is about 0·5 μg.

Hydrolysed fat-extracted *M. tuberculosis* by the above test showed a moderately strong D.A.P. spot corresponding to about 5·0 μg. Caseous tissue showed a spot of moderate strength (about 2·0–3·0 μg.); the Caplan nodule showed a faint but quite distinct spot (about 1·0 μg.), and a trace (about 0·5 μg.) was found in the non-caseous tuberculous lung. No D.A.P. was detected in the infective nodule, in the sample of progressive massive fibrosis, or in the normal lung.

Discussion

D.A.P. was first observed in *Corynebacterium diphtheriae* by Work (1949) and in *M. tuberculosis* by Asselineau and Lederer (1950). Subsequently many investigations have shown its wide occurrence in bacteria (see Work and Dewey 1953), but it has not been demonstrated in either tissue fluids or tissue hydrolysates of mammals.

The ability to demonstrate D.A.P. even in minute quantities in samples of lung tissue indicates heavy bacterial colonisation at some period in the evolution of the lung lesion. Since the method used cannot detect less than about 0·5 μg. of D.A.P., the concentration of this amino-acid in the positive specimens must have exceeded 1·5–2·0 μg. per mg. But D.A.P. only constitutes some 2% of the dry weight of those bacteria likely to occur in lung; 1·5–2·0 μg. therefore represents 75–100 μg. of dry bacillus weight. This is present in the residue after autoclaving; and, assuming that only negligible amounts of D.A.P. are extracted by autoclaving, evidence is thus obtained that lung lesions, despite the absence of cultural or histological evidence of infection, may contain identifiable bacterial residues resulting from a weight of infection amounting to at least 2·5% of the dry weight of the lesion itself.

Moreover, with the caseous material the strength of the D.A.P. spot suggested that the bacterial contribution to the lesion was much higher, amounting to at least 20% of the lesion. These figures must not be taken as evidence that bacterial debris is actually present to this extent, since the bulk of the organisms may well have been removed by the normal scavenging and enzymatic activities of the tissues. On this hypothesis D.A.P. should be a component of the highly resistant residue of the bacteria. That this is so for *M. tuberculosis* has been shown by Colover and Consden (unpublished) in a chemical study of the fraction of the tubercle bacillus that is active in the experimental production of allergic encephalitis (Colover 1954). An active residue remaining after prolonged extraction with fat solvents, followed by digestion with proteolytic enzymes, still contained D.A.P. in readily detectable amounts. Some mention should be made of presence of D.A.P. in the Caplan nodule and its absence in progressive massive fibrosis. Further investigation of the latter is necessary before this difference is established. Prior bacterial infection might be an important factor in pathogenesis of one or both of these conditions.

Two further aspects of these results are worthy of comment.

(1) The detection of bacterial debris by the presence of chemically characteristic components might well prove a useful method in the study of lesions of obscure ætiology, such as *sarcoidosis*. *The presence of either arabinose, rhamnose, or* mycolic acid would provide further confirmation of the presence of such bacterial residues.

(2) In view of the rôle of tubercle bacilli in the experimental genesis of immunity and allergy, the persistence in the tissues of resistant bacterial fractions might be of great significance.

Summary

A method is described for identifying α ε diamino pimelic acid in some lung lesions.

This amino acid was found in a caseous tuberculous nodule, a Caplan nodule, and a sample of non-caseous tuberculous lung tissue. It was not found in a sample of "progressive massive fibrosis" nor in an "infective nodule."

The bacterial residues in the caseous nodule represent a weight of infection amounting to about 20% of the dry weight of the lesion.

It is a pleasure to acknowledge the coöperation of Dr. J. Gilson, Dr. W. E. Miall, Dr. D. Rivers, and Dr. A. L. Cochrane, of the Pneumoconiosis Research Unit, for supplying tissues and for helpful discussion. The infective nodule was provided by Prof. J. Gough.

REFERENCES

Asselineau, J., Lederer, E. (1950) *C.R. Acad. Sci., Paris*, 230, 142.
Caplan, A. (1953) *Thorax*, 8, 29.
Clarke, H. B., Datta, S. P., Rabin, B. R. (1955) *Biochem. J.* 59, 209.
Colover, J. (1954) *Brain*, 77, 435.
Consden, R., Glynn, L. E., Stanier, W. M. (1953) *Biochem. J.* 55, 248.
— Gordon, A. H., Martin, A. J. P. (1946) *Ibid*, 40, 580.
Gomori, G. (1937) *Amer. J. Path.* 13, 993.
Miall, W. E., Caplan, A., Cochrane, A. L., Kilpatrick, G. S., Oldham, P. D. (1953) *Brit. med. J.* ii, 1231.
Work, E. (1949) *Biochim. biophys. Acta*, 3, 394.
— Dewey, D. L. (1953) *J. gen. Microbiol.* 9, 394.

SIMPLIFIED OPERATIVE ROUTINE FOR CARCINOMATOUS OBSTRUCTION OF COLON

B. N. Brooke
M.D. Birm., M.Chir. Camb., F.R.C.S.
READER IN SURGERY, UNIVERSITY OF BIRMINGHAM

For the treatment of acute colonic obstruction due to neoplasm it has been usual either to do the Paul-Mikulicz operation or to relieve obstruction with a colostomy, later resect the lesion, and finally close the phase of acute obstruction if the two stage procedure is planned It is to draw attention to the value of this method that the following three cases are reported

Case-reports

Case 1 —A woman, aged 70, was admitted on Feb 22, 1954, to the Queen Elizabeth Hospital with acute obstruction of the colon Laparotomy next morning revealed a mobile growth of the rectosigmoid A loop colostomy was constructed in the left iliac fossa as close to the lesion as possible After operation an infected hæmatoma formed in the wound Sixteen days after admission the abdomen was reopened through a low left paramedian incision, thus avoiding the previous site on the right side It was confirmed that the neoplasm of the rectosigmoid was at an early stage , no glands were palpable, and so anterior resection was undertaken The colostomy was detached from the abdominal wall and withdrawn into the abdominal cavity From that moment it was possible to do an anterior resection in the usual manner removing the growth within the pelvis after mobilising the upper rectum and ligating the superior hæmorrhoidal vessels , end to end anastomosis between the mobilised portion of the descending colon and the rectum at the level of the pelvic peritoneal reflexion was a simple matter after removing the sigmoid and rectosigmoid, which contained both growth and colostomy The operation was completed by suture of the laparotomy and colostomy wounds, the latter being drained Recovery was uneventful, and the patient returned home two weeks after the second operation

Case 2 was similar to case 1 as regards site of the neoplasm, but the technique of removal was somewhat different A man, aged 53, was admitted on March 24, 1954, with intestinal obstruction due to a growth found at laparotomy to be adjacent to the brim of the true pelvis The sigmoid loop was long , at the lowest possible site a colostomy was formed in the left iliac fossa After this operation the sigmoid tended to prolapse through the colostomy incision Ten days later the abdomen was reopened through the lower left paramedian incision Because of the bulk of colon exteriorised as the result of prolapse at the colostomy, it was decided to perform the dissection through the paramedian incision but deliver the resected portion through the colostomy wound, so as to avoid contamination which might result from returning the prolapsed portion and the colostomy to the abdomen The splenic flexure was mobilised, and since it was impossible to dissect in the lower part of the left paracolic gutter, the left colonic vessels were ligated at their origin from the medial side, and special care was necessary to avoid injuring the ureter An anterior resection was done with end to end anastomosis between the upper descending colon and the rectum The colostomy and the neoplasm were excised together in the length of colon removed through the colostomy incision The paracolic gutter was drained through the wound in the left iliac fossa which was repaired Convalescence was smooth and the patient returned home twelve days after operation

In Case 3, a woman aged 61, the lesion was at the splenic flexure The preliminary laparatomy was done through a lower left paramedian approach , and the colostomy, placed as far to the left in the transverse colon as possible was brought out above the level of the umbilicus through a left trans rectal incision Fourteen days later the left paramedian incision was reopened and was continued upwards to include the colostomy wound and detach the colostomy An excellent exposure was thus obtained, and left hemicolectomy was done with end to end anastomosis of the right trans verse colon to the lower sigmoid The paracolic gutter was drained through a stab incision in the flank, and corrugated rubber was placed at the site of the pre-existing colostomy The patient had an undisturbed convalescence and was discharged twelve days later

Management before resection in all cases has included colostomy washouts , and by mouth for three days streptomycin 1 g twice daily, alternatively oxytetracycline 250 mg six hourly, or phthalylsulphathiazole 2 g thrice daily, with the same drug instilled as a suspension into the distal loop of the colostomy At operation it has been found best to tie a dry swab over the colostomy and to make no attempt to close its opening with sutures, since this tends to be ineffective and promote bleeding and thus the possible spread of contaminants In the first case oxytetracycline, and in the second case streptomycin, was instilled around the area of dissection and anastomosis before closing the peritoneum This was done because of the wound infection complicating the one, and the prolapse increasing the possibility of contamination in the other , no local application of this sort was made in the third patient Case 1 was given oxytetracycline after operation because pus from the previous incision was encountered on reopening the abdomen No drugs of this sort were given to cases 2 and 3 after operation, and routine chemotherapy is avoided at this stage since these drugs are better kept in reserve for possible complications

The neoplasm itself has always been covered at an early stage with a surgeon's mask, the strings of which are tied tightly around the bowel above and below the lesion to prevent exfoliated malignant cells from spreading to the site of anastomosis, where they may be implanted (Cole 1952) while the mask itself prevents direct exfoliation and implantation due to manipulation

Conclusions

A method is described for treating carcinomatous obstruction of the colon and rectosigmoid At the initial operation to relieve obstruction, the colostomy is placed as close to the growth as possible so that both may be resected together at a second and final operation

The advantages include a reduction from three to two in the number of operative stages and therefore reduced risk of morbidity , shorter stay in hospital , and greater freedom of manœuvre, permitting wider excision of the area of lymphatic spread

REFERENCE

Cole, W H (1952) *Arch. Surg , Chicago*, 65, 264

PAROXYSMAL NOCTURNAL HÆMOGLOBINURIA

MARCHIAFAVA—MICHELI SYNDROME

David Douglas
M.D Glasg , F R F P S
CONSULTANT PHYSICIAN AND PHYSICIAN TO OUTPATIENTS
ROYAL INFIRMARY, GLASGOW

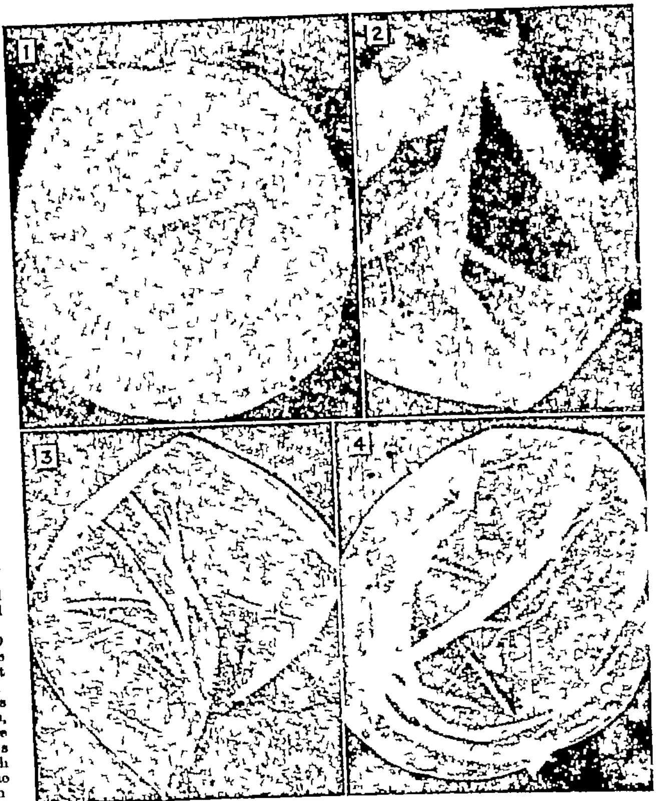
Jas C Eaton
B Sc , M.B Glasg , F R.I C
CONSULTANT BIOCHEMIST AND LECTURER IN PATHOLOGICAL
BIOCHEMISTRY IN THE UNIVERSITY OF GLASGOW

Chronic hæmolytic anæmia with paroxysmal nocturnal hæmoglobinuria (P N H) is fairly rare Crosby (195[illegible]) remarks that 162 cases have been reported since Marchiafava's first description in 1928, but probably the true incidence is much greater The ætiology is unknown The present concept is of a cell defect shared by erythrocytes, leucocytes, and platelets This defect of unknown nature but possibly one of cell stroma protein, renders the erythrocyte abnormally susceptible to a hæmolytic system present in normal plasma

It has been claimed that electron microscopy in some cases has shown abnormal structure in the envelope of the hæmolysed red cell (Matthes et al 1951) Electron microscopy in the case presented below did not support this contention

Case-report

A married woman, aged 35, with one child aged 11 years and no history of any previous illness of consequence, first noticed hæmoglobinuria in 1943 while she was pregnant She had it on only one occasion, but she was found, during the puerperium, to have a mild anæmia which did not respond to iron therapy She remained in her usual health thereafter until August, 1953, when she was admitted to hospital as a contact carrier of *Salmonella typhimurium* She was given a course of oxytetracycline, after which her stools were negative



Appearance of normal and P N H erythrocyte ghosts on electron microscopy: 1 normal erythrocyte unshadowed (× 8000); 2, P N H erythrocyte unshadowed (× 12,000); 3 normal erythrocyte shadowed with Au and Pd (× 8000); 4 P.N H. erythrocyte shadowed with Au and Pd (× 8000)

pathogens. She was again found have an anæmia not responding iron. Shortly afterwards hæmo bulinuria recurred being present the first morning specimen of ne but not at other times of the y Her doctor detected slight ndice which remained, with me fluctuation until readmission hospital in December 1953 The tient felt tired and weak and d spells of dizziness in the morn g lasting about an hour She new by a feeling of general malaise hen she would pass bloodstained rine. There was no history of næmia or jaundice in her family r of exposure to hæmolytic drugs

The patient was a small and slimly built young woman who was pale and had a lemon yellow tint and a few soft and slightly enlarged glands on either side of the neck but not elsewhere No enlargement of liver or spleen was detected No abnormality was found in the cardiovascular respiratory nervous or alimentary systems. The morning urine was the colour of port wine and contained albumin but no bile

Laboratory Investigations.—Examination of the blood showed Hb 9·8 g per 100 ml red cells 3,030 000 per c.mm., and white cells 5400 per c.mm A red-cell fragility test showed that hæmolysis began in 0·5% solution and was complete in 0·35% (control 0·45% and 0·4% respectively) The blood group was A Rh D positive The probable genotype was R2 r (c̄DE c̄de) The direct Coombs test was negative; and when the patient's serum was tested against a large panel of cells, no irregular antibodies were detected Ham's test and Crosby's modification of Ham's test both showed strong hæmolysis of the patient's cells by homologous serum whereas there was no hæmolysis in the control tests. In addition the patient's cells were incubated with an anti A serum which contained a weak anti A hæmolysin; the control cells showed slight hæmolysis, whereas the patient's cells were considerably hæmolysed The Wassermann and Donath Landsteiner tests were negative Between periods of hæmoglobinuria the serum contained small amounts of oxyhæmoglobin and considerable amounts of methæmalbumin Shortly after the passing of dark urine it contained a large amount of oxyhæmoglobin and a small amount of methæmalbumin. The methæmalbumin was never demonstrable spectroscopically and was only detected by plotting absorption curves on a spectrophotometer Electrophoresis of the serum did not reveal any abnormality; likewise electrophoresis of the hæmoglobin within the cells revealed no difference in mobility from that of control samples The dark samples of urine contained variable amounts of methæmoglobin and oxyhæmoglobin. When the urine was freshly passed the amount of methæmoglobin was usually considerable but on standing it disappeared rapidly increasing alkalinity converting it to oxyhæmoglobin. The deposit revealed a few hyaline casts numerous squamous epithelial cells (a small proportion of which contained iron granules within the cells) and very numerous amorphous particles of iron-containing material. No red blood-cells were seen. The urinary excretion of urobilinogen was 3 mg daily The fæces were of normal colour The fæcal excretion of urobilinogen was 238 mg daily

Progress.—Hæmoglobinuria ceased spontaneously after five weeks. It has not so far recurred but there has been no improvement in the anæmia. The patient's general condition remains moderately satisfactory There have been no thrombotic or infective complications For these reasons it has not been deemed advisable to give a transfusion of washed cells or anticoagulant drugs which may have a temporary ameliorating effect on hæmolysis

Electron Microscopy.—The patient's red cells were examined by electron microscopy and some of the results are shown in comparison with those of normal cells in the accompanying figure The cells, obtained from samples prepared as shown below were separated from plasma or from serum by spinning and hæmolysed with 5 10 or 30 volumes of water The envelopes were separated by centrifuging and were treated with 1% osmium tetroxide for 30 minutes The material was again spun, washed resuspended to a suitable concentration and sprayed on to a supporting film for microscopy Some films were shadowed with gold and palladium at 15 C The following preparations were examined thus: (1) citrated blood; (2) cells from blood allowed to clot spontaneously; (3) cells from blood defibrinated by shaking with glass beads (4) cells from blood defibrinated by stirring with a glass rod; (5) as (3) but after allowing the blood to stand for some days before defibrinating; and (6) as (4) but allowing the blood to stand for some days. Samples 4 5, and 6 were unshadowed None of the photographs showed any significant differences between normal and P.N.H cells. There was no evidence of the spotty or "mesh like" appearance described by Matthes et al (1951)

Discussion

The lytic mechanism in P N H has been studied by many workers, notably Crosby (1953) and Crosby and Bell (1951), the current views and the literature being well reviewed by Crosby (1953) It has been shown that both lytic and inhibitory factors are present in normal plasma, but that the abnormality in P N H does not lie in these factors If P N H cells are placed in normal plasma they tend to undergo lysis, this process being hastened by acidification, normal erythrocytes are not lysed by P N H plasma This explains why transfusion of a P N H patient with normal blood tends to produce a lytic crisis The system present in the normal transfused plasma attacks the abnormal cells of the patient If washed cells only are given, the normal plasma system being absent, no lysis results

Despite much examination no satisfactory explanation is forthcoming for the widely observed tendency of P N H patients to get lysis during sleep It has been repeatedly suggested that diminished excretion of respiratory carbon dioxide during sleep reduces the plasma pH (T H Ham 1939, G C Ham and Horack 1941, Matthes et al 1951), but the evidence for this is not entirely conclusive (Peterson 1949, Crosby and Bell 1951) From in-vitro experiments Peterson (1949) suggested that carbon dioxide has some specific effect not shared by other acids, but Crosby and Bell (1951) and Ham (1939) could not confirm this It appears clear that the lytic tendency is associated with sleep as such and not with posture or time of day Increase of pulmonary ventilation in a respirator during sleep will prevent lysis (Ham 1939, Ham and Horack 1941)

Paroxysmal nocturnal hæmoglobinuria does not appear to be hereditary, only one of a pair of uniovular twins had the abnormality (Crosby 1953) The onset is usually in adult life, the sexes are equally affected It has been suggested that the disease is due to some unknown sensitisation Experiment has failed to reveal any abnormality in the hæmoglobin (McIlvaine and Beard 1951 and our own results) The apparently normal condition of plasma and hæmoglobin in this disease points to the red-cell envelope as the seat of the abnormality Despite the claim by Matthes et al (1951) to have demonstrated lacunæ and a mesh like appearance in electron microphotographs of P N H cells, our findings showed no significant difference between P N H and normal cells Sundharagiati and Wright (1953) found changes similar to those described by Matthes et al in a variety of blood dyscrasias and believe that these were due to artefacts

Splenectomy has been found to be useless or even harmful Treatment with alkali is ineffective (Buell and Mettier 1940), and numerous hormones and drugs have been tried without success by other workers Crosby (1953) showed that dicoumarin may help Thrombin destroys the normal heat stable inhibitor of lysis By preventing conversion of prothrombin to thrombin dicoumarin inhibits this destruction In emergency, transfusion with homologous cells washed free from plasma is effective

Summary

A case of paroxysmal nocturnal hæmoglobinuria is described

The laboratory findings were characteristic Some hæmolysis was present even when there was clinical remission Electrophoretic examination of the hæmoglobin revealed no abnormality Electron microscopy of the lysed red blood-cells showed no difference between their envelopes and those of normal erythrocytes

We wish to thank Miss H. M Laird, of the Beatson Memorial Hospital, f [illegible]eparing and reporting on the electron micro photographs, Dr J Wallace, of the West of Scotland Bl Transfusion Service, for serological examination of the bloo and Dr David Smith, of Glasgow Royal Infirmary, permission to examine the patient

REFERENCES

Buell A. Mettier, S R. (1940) *J Lab clin Med* 26, 1434
Crosby, W H (1953) *Blood*, 8, 769
— Bell, J C (1951) *Rev Hémat* 6, 299
Ham, G C, Horack, H M (1941) *Arch intern Med* 67, 735
Ham, T H (1939) *Ibid*, 64, 1271
McIlvanie, S K, Beard, M F (1951) *Blood*, 6, 936
Marchiafava, E (1928) *Policlinico, sez med* 35, 109
Matthes V M, Schubothe, H, Lindemann, B (1951) *Acta ha*
5, 193
Peterson, A (1949) *Dtsch Arch klin Med* 196, 486
Sundharagiati, B, Wright C S (1953) *J clin Invest* 32 979

ON THE SEX OF CANCER AND TERATOMATA CELLS

AMÂNDIO S TAVARES
M B Oporto
ASSISTANT, DEPARTMENTS OF GENERAL AND ANATOMICAL PATHOLOGY, FACULTY OF MEDICINE, OPORTO UNIVERSITY, PORTUGAL

A MORPHOLOGICAL sexual difference in the nucle nerve-cells of cats was found by Barr and Bertr (1949, 1951), and later work showed that a chromat mass called "sexual chromatin" or "corpuscle of Barr is seen in about 75% of nuclei of various tissues in femal but is seldom detected in males (Barr et al 1950, Grah and Barr 1952)

These findings have been applied to the diagnosis sex in other animals and in man (Moore and Barr 195 For instance, nuclear sex has been studied by th method in transvestites (Barr and Hobbs 1954), herm phrodites (Moore et al 1953, Barr 1954), and Turne syndrome (Polani et al 1954) Using a slightly modifi technique, Emery and McMillan (1954) say that, exce for some doubtful results obtained in necropsy mater in the newborn, the method is reliable when applied children

Hunter and Lennox (1954), who examined spin cellular epitheliomata of the skin, conclude that canc cells are of the same sex as the patient, but, as regar teratomata, 5 out of 9 in males were heterosexu whereas 12 teratomata in women were all of the sam sex as the patient If this latter finding is applicab generally, we will have to revise our ideas of the genes of teratomata

Meanwhile we add to the findings of Hunter an Lennox (1954) and of Cruickshank (1955) our finding in 34 teratomata and 110 cancers

Method

We used formalin fixed paraffin embedded section 5–8 μ thick stained with hæmatoxylin and eosin, and

TABLE I—SEX OF CANCER CELLS

Tumour	Sex of patient					
	Male			Female		
	Average (%)	no of cases	Range (%)	Average (%)	no of cases	Rang (%)
Carcinoma of skin	5 9	24	1 5–17 0	72 9	27	[illegible]
Undifferentiated carcinoma of skin		2	1 0– 4 0		3	[illegible]
Primary carcinoma of liver		1	11 5		3	[illegible]
Adenocarcinoma of stomach	5 6	5	2 5– 9 5	69 8	5	[illegible]
Papillary carcinoma of bladder	6 4	5	3 0–12 0	70 2	5	[illegible]
Adenocarcinoma of ovary				73 3	5	[illegible]
Seminoma of testis	4 0	5	3 0– 5 5			
Carcinoma of kidney	7 5	5	4 0–11 0	71 9	5	[illegible]
Myosarcoma	8 6	8	5 5–15 0		2	[illegible]

TABLE II—SEX OF TERATOMA CELLS

Sex of patient	Sex of teratoma cells							
	Male				Female			
	Hunter and Lennox (1954)	Cruickshank (1955)	Present investigation	Total	Hunter and Lennox (1954)	Cruickshank (1955)	Present investigation	Total
F					12	2	25	39
M	4	2	5	11	5	1	4	10
Total	4	2	5	11	17	3	29	19

χ^2 (for 1 : 2 ratio) = 1·999 P = 0·166
χ^2 (for 1 : 1 ratio) = 0·0476 P = 0·962

controls were stained by the Feulgen method We found fixation to be of greater importance than the method of staining

Counts were made of nuclei containing the sexual chromatin, as defined by Barr and his colleagues, and percentages were established for at least 200 cells doubtful nuclei were counted as half positive half negative Immature and degenerated cells were excluded and only one nucleus was examined in the multinucleated elements so commonly found in cancer

This method gave statistically significant results ($P = 1 \times 10^{-11}$) with a relatively small standard deviation ($s = 2·5$) In the case of normal skin cells of 40 adults the sexes being well separated (females 60–80% males 1–18%) and the two frequency curves showing diverging skewness.

Results

Cancer

In 110 sundry malignant tumours, taken at random for each variety from the cases registered in the department of anatomical pathology in the University of Oporto the sex of the patient and that of the tumour were the same (table I) The range of results shows no significant difference between normal and cancer cells and identical percentages were obtained when both were examined in the same section Neither localisation nor type of neoplasm influenced its 'sex' the only exceptions were two undifferentiated carcinomata of the skin in women the low figures (27% and 55·5%) may be explained by the immaturity of the nuclei in these neoplasms.

The number of chromatin containing cancer cells and mature histiocytes in the stroma of the tumour were counted in 20 cases and differed very little ($t = 0·632$ d f. = 10) The histiocytes proved much more reliable than epithelium because in the undifferentiated carcinomata mentioned above the histiocyte-counts were 70·0% and 74·5%

Teratomata

Our findings in 34 teratomata (25 from women and 9 from men) were very similar to those of Hunter and Lennox (1954) all 25 from women were 'feminine' whereas 4 of the 9 from men were 'masculine' If we combine our findings with those of Hunter and Lennox (1954) and Cruickshank (1955) we find that 48% of teratomata in males are heterosexual This fact argues against two current theories of the genesis of teratomata: the blastomere theory and that of parthenogenetic division of a diploid cell On the other hand not much support is lent to the theory of gamete (or at least haploid cell) conjugation proposed by Hunter and Lennox (1954) which calls for a ratio of 1 XX : 2 XY : 1 YY teratomata According to Moore and Barr (1954) only the pair of XX chromosomes determine the appearance of sexual chromatin This reduces the genetic ratio to 1 XX : 3 (XY + YY) or if YY cells do not survive (and we know very little on this subject) to 1 XX : 2 XY The χ^2 test of departure gives a probability rather close to the statistical level of significance (table II)

The objection that teratomatous material, since it is often either undifferentiated or immature is unsuitable for this study does not hold at least for our series only nuclei from mature epithelial connective and nervous tissue were counted On the other hand, if lack of cell differentiation (which may only cause a depression in percentages as we have shown) influenced our results, these would be reversed and heterosexuality would be found in women alone

A far greater number of teratomata will have to be studied before any theory emerges from these findings However, one explanation of a 1 : 1 ratio is perhaps, the parthenogenetic division of haploid cells followed by chromosome reduplication, forming 100% of XX cells in the female, and 50% of XX and 50% of YY cells in the male Of course this means attributing a pair of YY chromosomes to the cells of some teratomata, and we do not know anything about their viability

REFERENCES

Barr M L (1954) *Surg Gynec Obstet* 99 184
— Bertram E G (1949) *Nature Lond* 163 676
— — (1951) *J Anat* 85 171
— Bertram L F Lindsay H A (1950) *Anat Rec* 107 253.
— Hobbs G E. (1954) *Lancet* i 1109
Cruickshank, D B (1955) *Ibid* i 253.
Emery J L McMillan M (1954) *J Path Bact* 68 17
Graham M A Barr M. L (1952) *Anat Rec* 112 709
Hunter W F Lennox, B. (1954) *Lancet* ii 633
Moore K L Barr M. L. (1954) *Acta anat* 21 187
— Graham M A., Barr M. L (1953) *Surg Gynec Obstet* 96 641
Polani P E., Hunter W F Lennox B (1954) *Lancet*, ii 120

LOCAL TRANSMETATARSAL AMPUTATION IN ARTERIAL INSUFFICIENCY OF THE LOWER LIMB

A. G NORMAN

M.A., M B Camb F.R C.S

SENIOR SURGICAL REGISTRAR, ST THOMAS'S HOSPITAL, LONDON

ARTERIAL insufficiency of the lower limb is nowadays treated more conservatively than formerly preserving as much of the limb as is compatible with healing and sound function In gangrene of the foot amputation at the metatarso phalangeal joint commonly proves unsatisfactory and in the past these unsuccessful cases were treated by high amputation We now attempt to save more limbs by local transmetathrsal (ray) amputation

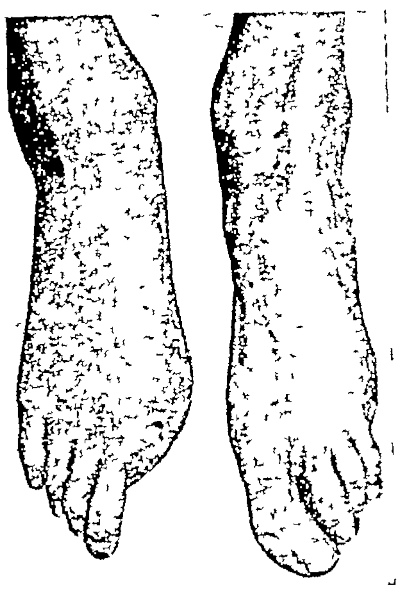
In the present series of 12 cases involving 14 limbs with gangrene of toes only one of the five toes was involved in 10 limbs This suggests that there must be some *local fault in the circulation of the affected toe* Our arteriographic studies have led us to believe that gangrene in the arteriosclerotic patient results from multiple blocks and we suspect that in these cases the final block is in the plantar metatarsal arteries as they pass the head of the metatarsal bones (Rob 1954) Although the *toes, unlike the fingers* have both dorsal and plantar digital arteries it is the plantar arteries that carry *most of the blood supply*

In local transmetatarsal amputation the toe and the head of the corresponding metatarsal bone are removed through an anterior racket incision The aim is to amputate above the level of the arterial block Great care must be taken to clear away all splinters of bone since these if unremoved, delay healing

Of the 12 patients (9 men 3 women) whose average age was 61·5 all had diffuse arterial disease and 5 were diabetic The main manifestations in the 14 affected limbs were: dry gangrene (6 cases) ulceration (5), and cold blue toe (3), and the average length of history was four months In 5 cases these manifestations had been preceded by claudication in the calf

The digits most commonly affected were the first, fourth, and fifth The numbers affected in the 14 limbs were first digit, 4, second digit, 1, third digit, 1, fourth digit, 7, and fifth digit, 5

The results at three to fifteen months after operation were as follows healed, 7 (primary healing 5, delayed healing 2), unhealed, 2, required high amputation, 5 Thus the failure rate was 36%, which is similar to the 37% in a series of total transmetatarsal amputations described by Warren et al (1952)



Foot after local transmetatarsal amputation of right first toe and left fifth toe

Analysis does not reveal any sign by which failure can be predicted Failure was unrelated to age, sex, or the presence of diabetes

This operation is designed to remove as little as possible of the gangrenous limb McKittrick (1946), McKittrick and Risley (1949), Furste and Herrmann (1948), and others have attempted to achieve this end by total transmetatarsal amputation, thereafter the foot functions well (unlike the state after amputations at the tarsus by the method of Lisfranc and Chopart), and their results are similar to those described here

After local transmetatarsal amputation the healed foot (see figure) is functionally satisfactory, and the limited follow up in the series described here shows that the wound remains satisfactorily healed In 1 of the diabetic patients a perforating ulcer of the foot developed, but the amputation site remained healed

I am indebted to Prof George Perkins for introducing me to this operation, to Mr F B Cockett for criticism and advice, to the physicians and surgeons of St Thomas's Hospital for permission to describe their cases, and to Mr K G Moreman for the photograph.

REFERENCES

Furste, W , Herrmann, L G (1948) *Arch Surg , Chicago*, 57, 15
McKittrick, L S (1946) *New Engl J Med* 235, 929
— Risley T S (1949) *Ann Surg* 130 826
Rob G C (1954) *In* Recent Advances in Surgery Edited by H. C. Edwards London p 329
Warren, R , Crawford, E S , Hardy, I B jun McKittrick, J R. (1952) *Surgery* 31, 132

Medical Societies

ASSOCIATION OF CLINICAL PATHOLOGISTS

THE 54th meeting of this association was held in Douglas, Isle of Man, on April 13–15 We publish summaries of some of the papers presented at the meeting

Typing in Epidemiological Investigations

Dr W H **BRADLEY** said that Griffith had first introduced serological typing of hæmolytic streptococci in 1926, and by 1934 a range of 27 reference types was available Craigie and Felix had shown in 1938 that bacteriophage typing of *Salmonella typhi* was practicable, and by 1947 they had prepared a couple of dozen reference phages The significant fall in the mortality of streptococcal disease (particularly puerperal sepsis) between 1934 and the advent of sulphonamides probably reflected the increase in the possibility of outbreak control stimulated by the Griffith's typing

The mortality of enteric fever in the United Kingdom had fallen away more rapidly than in other European countries, and this improvement coincided with the introduction of phage-typing Dr Bradley thought that because typing made epidemiological investigations more convincing and more fun their quality was improved and preventive medicine became more effective Moreover, epidemiological and ætiological concepts had been reshaped The rôle of type 12 and to a lesser extent type 4 streptococci in nephritis was an example It was now realised that the many distinct serological or phage types within a species were acting independently and that their specificity was enduring

Antigenicity of Toxoids and Sympathomimetic Drugs

Dr J **UNGAR** described how water insoluble mineral carriers such as aluminium or calcium salts, tapioca, oils and fats, and, recently, bacterial suspensions, had been used to increase the efficiency of prophylactic toxoids and thereby reduce the number of injections required Their presence caused local irritation, which was most severe with aluminium and calcium salts and least severe with bacterial suspensions, he had used *Hæmophilus pertussis* vaccines successfully in the past

As the use of vaccines might be undesirable in hypersensitive persons, Dr Ungar had tried to improve the antigenic efficiency of diphtheria toxoid by altering the rate of absorption with drugs exerting a local tissue effect Adrenaline hydrochloride (1 in 1000 to 1 in 2000), benzedrine hydrochloride (1 in 250), ephedrine hydrochloride (1 in 250), and histamine (0 5 µg per ml) had been used Two amines, β phenylethylamine and phenylethylamine acetate, which have no vasoconstrictor action, were included as controls When tested in guineapigs the sympathomimetic vasoconstrictors greatly enhanced the response to diphtheria toxoid Combination with histamine caused only slight enhancement and the two control amines did not affect the response to the toxoid Vasoconstrictors might prove useful for enhancing the efficiency of diphtheria toxoid, especially when children hypersensitive to injections of antigen were being immunised

Lung Carcinoma in Hæmatite Miners

Dr J **STEVEN FAULDS** said that the incidence of primary cancer of the lung in iron ore miners in Cumberland over the last twenty three years was 9 4%—four times that found in a control group of males of similar age and habits, but different occupation. The site of the tumours corresponded to the areas where the characteristic massive fibrosis developed, and the primary lesion was not in the main bronchus, but in a peripheral lung field The observed association of squamous celled lining to a chronic abscess cavity and a squamous carcinoma in the same area suggested that the tumour arose in the sidero silicotic mass Since silicosis was a frequent finding in other kinds of mining and an association between silicosis and bronchial cancer was not common, it was difficult to give a reason for the increased frequency of carcinoma found in iron ore miners

Lower-nephron Nephrosis

Dr S **SEVITT** showed that distal tubular necrosis (lower nephron nephrosis) in the kidneys of burned patients was commoner among those who had an adequate or normal flow of urine than in those with severe oliguria or anuria Clinically and biochemically there were uræmic and non uræmic forms with little or no oliguria The uræmic group was important to diagnose because the recent advances in therapy may reduce its high fatality Morphologically these kidneys showed a *diffuse* distal tubular neurosis in which hæmoglobin casts were prominent Many nephrons were involved and although the morphology was no different from that found in those with anuria or severe oliguria, tubular function was impaired

The finding of non-oliguric uræmia in an injured man with histological distal tubular necrosis of the kidneys indicated that the phenomenon was not restricted to burned subjects In the non uræmic condition there was no significant azotæmia during the illness, and death was due to non renal complications. Histologically the kidneys of these patients should show either a *focal* type of distal tubular necrosis, associated with few casts and affecting only a minority of the nephrons, or the healing or healed evidence of a recent focal attack.

Blood-ammonia Levels in Liver Disease

Mr A G Riddell described experiments on dogs with portacaval anastomoses which had shown that a neurological disorder can be produced in these animals by intoxication with ammonia Histological examination of the brains of these dogs showed the same change in the protoplasmic astrocytes as in patients dying in hepatic coma In hepatic coma a raised blood ammonia level was found The type of hepatic coma that followed bleeding from œsophageal varices was analogous to the syndrome seen in dogs and the ammonia was derived from the blood in the alimentary tract While blood ammonia determinations were required in the diagnosis and management of unusual cases, they were not required in the routine treatment of hepatic coma.

Fibrinous Vasculosis

Dr A. C Lendrum suggested this term for the deposition in blood vessel walls of a material giving the staining reactions of fibrin. The commonest cause of this was severe stagnant ischæmia, as in infarction or torsion Other causes were drug-induced hyperergic arteritis extreme hypertension, polyarteritis nodosa and occasionally acute rheumatic disease disseminated lupus erythematosus and dermatomyositis The fibrin was commonly seen under an intact endothelium sometimes as a complete ring round the intima From this level it either seeped into the wall (vessels of infarcted zone) or was injected across the media (in extreme hypertension) to spread out along the external elastica through which it may erupt focally At sites where a layer was traversed, there was in all types of fibrinous vasculosis a stretching and distortion of the nuclei as if they had been subjected to mechanical extension. Gross cellular aggregation was seen in and around a few some or all of the affected vessels. Intravascular thrombosis was uncommon except in small vessels, even when the vessel wall was a mass of fibrin

The most extreme degree of fibrinous vasculosis had been seen in the pulmonary vessels in 2 cases of mitral stenosis; and the next degree in infarcted organs. The three forms of fibrinous vasculosis, the stagnant hypertensive and hyperergic, appeared to be histologically indistinguishable. All might be regarded as a form of exudation due to an upset between the pressure in the vessel and the permeability of the lining

Hæmophilia and Christmas Disease

Dr Rosemary Biggs discussing the diagnosis of these conditions, said that the laboratory tests of clotting function that have been used were the whole blood clotting time the prothrombin-consumption test and the thromboplastin generation test. In hæmophilia the clotting time was prolonged in more than half of the patients, but patients who are quite severely affected may have a normal clotting time Similarly the prothrombin-consumption test usually gave abnormal results in hæmophilia, but with some samples results were normal The thromboplastin-generation test gave more reliable results in hæmophilia blood than either of the other tests, and using this technique it was possible to distinguish patients with hæmophilia from those with Christmas disease About 10% of patients previously diagnosed as having hæmophilia were found to have Christmas disease Of the patients with Christmas disease many were rather mildly affected with a normal clotting time and consumption of prothrombin

Interstitial Emphysema in the Newborn

Dr John L. Emery in a consecutive series of 100 infants dying within seven days of birth had found that 7 out of 5[illegible] full term children had died with interstitial emphysema After congenital deformities it was the commonest single cause of death The condition was spontaneous and not due to artificial respiration it was probably caused by the expulsive efforts of crying in lusty infants who had inhaled vernix or mucus.

OPHTHALMOLOGICAL SOCIETY OF THE UNITED KINGDOM

Diamox in the Treatment of Glaucoma

The 75th congress of the Ophthalmological Society of the United Kingdom, held in London on April 28–30 included a symposium on Diamox' in the Treatment of Glaucoma Diamox (2-acetylamino 1 3 4 thiadiazole 5 sulphonamide) has been known for some years to have a powerful inhibitory effect on the enzyme carbonic anhydrase and it has been used in the treatment of congestive heart-failure because of its diuretic effect [1]

Mr E S Perkins analysed the results in 58 cases treated at Moorfields Eye Hospital, and confirmed the value of this drug in controlling all of the major categories of glaucoma in about 50% of all cases—congestive glaucoma, simple glaucoma and glaucoma secondary to iritis and to trauma—the tension was brought well under control while of the remaining cases about half were controlled partially or for a short period This effect was potentiated by the simultaneous use of miotics The dosage suggested was 500 mg initially followed by 250 mg six hourly after a few days this dose could generally be reduced to twice or thrice daily at which level it should be maintained Side-effects were rarely disturbing diuresis and paræsthesiæ were usually very transient Mr Perkins concluded that the particular value of diamox was in the control of acute congestive glaucomatous crises where it allowed the eye to quieten for a subsequent drainage operation; in certain cases of simple glaucoma where miotics had failed to achieve effective control, and in cases of iritis glaucoma in which the tension could be controlled until the initiating iritis had been allayed

Dr John Gloster described his estimation of the effect of diamox on the intra-ocular pressure of normal rabbit eyes. He found that an intravenous injection of diamox caused a drop in the intra-ocular pressure within one minute the speed of this action suggested that it was due to a direct effect on the secretion of aqueous humour in the ciliary body The changes estimated by the insertion of a cannula into the aqueous, were significant only with doses larger than those used clinically

Dr Maurice Langham reported the results of further experiments on rabbit eyes Observations were made first on the effect of diamox on the distribution of bicarbonate between the aqueous humour and the plasma, since it might be assumed that the inhibition of the production of hydroxyl ions would decrease the osmotic pressure of the aqueous and thereby reduce its formation The influence of the drug was assessed according to the permeability of the blood aqueous barrier and the flow of the aqueous humour by measuring the rate of accumulation of fluorescein in the aqueous humour after intravenous administration It was found that although the bicarbonate in the aqueous diminished after the administration of diamox its concentration relative to that in the plasma was unchanged The method by which diamox reduced the formation of the aqueous thus remained uncertain; the results of his experiments did not show whether diamox in fact exerted its effect by its systemic action or through a non specific inhibition of aqueous secretion

Prof G P Sourdille (Nantes) reported clinical observations which agreed essentially with those described by Mr Perkins

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[1] See *Lancet* April 2 1955 p 706

Reviews of Books

Practical Obstetric Problems

IAN DONALD, M B E , M D Lond , M R C O G , regius professor of midwifery, University of Glasgow London Lloyd-Luke 1955 Pp 578 45s

IN many ways this is an admirable book, but it is not addressed consistently to any particular group of readers, and one cannot easily say just what kind of book it is. The title and part of Professor Donald's preface suggest that it is largely a reference work for the practising obstetrician, but, though the practising obstetrician will find much profit and enjoyment in its discussion of controversial problems, it leaves out things one would expect it to contain It is not a textbook, for the anatomical and physiological ground-work of obstetrics has been deliberately omitted Perhaps it will be of most value to those who have a little experience of obstetrics and are sitting a higher examination —though these will have no need of the details of simple obstetrical procedures (such as toilet of the vulva before forceps delivery) nor of some of the discussions of matters that belong to undergraduate rather than postgraduate teaching

The points at which fellow experts will take issue with the author mostly concern manipulative obstetrics In the section on manual correction of the fœtal head in the occipito posterior position, a good method is described for altering the fœtal position, but no reference is made to the alternative techniques, such as rotating the shoulders by the internal hand or correcting the malposition by placing the hand over the fœtal face In the section on breech delivery the description of the rotation of the anterior shoulder posteriorly does not mention the desirability of over correction if the back of the fœtal head is to remain directed to the symphysis The statement that "the lateral position for forceps delivery has been abandoned" takes no account of those who are convinced that the lateral position confers at least the two advantages of a reduced risk of anæsthesia and less perineal damage Some, too, will disagree with the opinion (on twins) that "if a general anæsthetic has been necessary in the course of delivery of the first child it is usually preferable to discontinue it while awaiting the arrival of the second." Sweeping statements such as "Cæsarean myomectomy is an indefensible operation" and "undoubtedly" routine X ray pelvimetry in all primigravidæ "will come in time" belong perhaps to the cut and thrust of debate rather than to the printed page

Against these objections must be set the important fact that the book conveys much of the author's zest Some of its parts, and some of its sentences, are too long, but it is often very readable Many will be grateful for its robust, uncompromising approach, and above all for its stimulating enthusiasm

Memoirs of My Nervous Illness

DANIEL PAUL SCHREBER Translators and editors IDA MACALPINE, M.D , RICHARD A HUNTER, M.D , M.R C P , D.P M London Wm Dawson 1955 Pp 416 £1 15s

AUTOBIOGRAPHICAL accounts of mental illness are valuable documents, especially when written by patients of high intelligence, gifted with powers of self-observation and accurate recollection These qualities were undoubtedly possessed by Daniel Schreber, a judge of the supreme court in Saxony, who developed a severe schizophrenic illness in late middle life His account of his experiences in this illness, first published in 1903, was the subject of a study by Freud eight years later Freud's paper has become important in the development of psycho-analytic theory about psychoses, and the Schreber memoirs are often mentioned, but usually by people who have not read them, because the book has become scarce and has never been translated from German Dr Macalpine and Dr Hunter have now made good this deficiency

Their translation does not always run smoothly, but it may well be a faithful reproduction of Dr Schreber's style Schizophrenics do not write with terse and graceful precision, nor perhaps do judges, and the reader is willing to accept the translators' disconsolate reference to Schreber's cumbersome and involved language They give examples of his neologisms in an appendix They have fallen into a few well known traps—such as translating *Moment* as "moment" instead of "factor"—but these are trifling blemishes in a large undertaking Besides the memoirs, the book contains a clinical and historical introduction by Dr Macalpine and Dr Hunter, a reprint of their informative psychopathological article on the Schreber material, and translations of the psychiatric reports on Schreber, the legal statement in which he asked to be given back control over his affairs, and the judgment of the court which heard this appeal.

The translators ride a few hobby-horses, as their incidental polemic against physical forms of treatment shows, but the grateful reader will not begrudge them this by-product of their labours for his benefit, he may even, unless an orthodox psycho-analyst, find their irreverent re-examination of some central issues of Freudian psychopathology stimulating

Examen clinique et traitement d'un endocrinien

A. LICHTWITZ and R PARLIER, Hôpital Lariboisière Paris Paris L'Expansion scientifique française 1954 Vol I Pp 456 Fr 5200 Vol II Pp 302 Fr 4800

To apply recent advances in endocrinology demands some understanding of the experimental techniques which produced them Doctors are often ill equipped by their training to follow the methods of diagnosis and treatment that have evolved Dr Lichtwitz and Dr Parlier, in this frankly didactic account of endocrinology in its modern setting, have, by their attention to layout, tables, and diagrams, done much to explain the scientist's findings to the clinician In the preface they write "We hope the jealous guardians of pure biological science will pardon certain abuses of simplification, remembering that our aim is to reach not only those doctors who wish to perfect their knowledge of modern endocrinology, but all those who are harassed by the problems of general pathology" But the questioning and thoughtful reader may be disappointed

Dr Lichtwitz and Dr Parlier deal first with some general principles and then with the hypophysis, the thyroid, the ovary, and, in the second volume, with the testes and the suprarenal Throughout, the influence of Selye makes itself strongly felt The book is a useful guide to the French literature and in particular to the authors many original articles. It is lavishly produced, and misprints are mostly in the references but the index is unfortunately sketchy

The Challenge of Man's Future

HARRISON BROWN London Secker & Warburg 1954 Pp 290 21s

Prof Harrison Brown is a chemist with an expert's knowledge of the earth's material resources, an American's optimism about human capacity, and a citizen of the world's awareness of the rake's progress and the fateful hour Like Sir Charles Darwin he sees the ultimate consequence of an uncontrolled growth of population and a spendthrift use of our resources, but he is not convinced that there is no escape from this doom

He foresees three possible patterns of life reversion to the agrarian existence of the pre-industrial period a completely controlled, collectivised industrial society in which war has been abolished, new energy sources are utilised, and population is kept stable, a world wide free industrial society, labile but capable of permanence The last, the most desirable and to our favoured Western minds the expected outcome of "progress," is the most difficult to achieve since it requires efforts beyond anything human beings have so far compassed They must adapt themselves to constant change, preserve freedom while accepting control of reproduction, aggression, and other old desires, and use their intelligence and self-restraint now in order to conserve their dwindling extra-human resources and so turn to most use their inner resources of wisdom and generosity Though this is the conclusion of the matter, and gives only chastening comfort, it follows a well-organised factual account of what is happening and what must later happen if we continue in our present courses the account is objective and the main argument irrefutable

THE LANCET

LONDON SATURDAY, MAY 7, 1955

Research in General Practice

> There is a danger inherent in the work of general practice that the very great variety of subjects for practice and thought in a day's work may lead to a superficial and desultory curiosity rather than an eagerness for study.

WHEN he offered this reflection in the first John Matheson Shaw lecture[1] of the Royal College of Physicians of Edinburgh last November, Prof. JAMES MACKINTOSH was discussing the opportunities for research now opening before general practitioners. A Sassenach might have softened the blow with some reference to the fatigues of the family doctor's day, but Professor MACKINTOSH merely added that "it is easy to spread a thin layer of butter on the bread of idleness." This bracing approach has much to commend it, for some of the past attempts to get general practitioners to contribute to research have started hopefully but died of inanition. Too often self-chosen projects lose their charm for men working in isolation, especially during winter epidemics. Modern research is often done best by a team, and the College of General Practitioners[2] is surely right in encouraging group projects while at the same time offering information and help to the investigator who prefers to work alone.

At the end of 1954, the register of members willing to take part in research maintained by the research committee of the college council, contained some 380 names, sent in from every part of the Commonwealth. Research committees of 22 faculty boards have been formed in the British Isles and overseas composed of members and associates of the college and also coöpted members from local university or medical-school research departments. The college research advisory panel composed of experts in various medical fields, has been strengthened during the year. Scotland has its own research committee of the Scottish council with its own research advisory panel.

Four types of general practitioner research are being forwarded: college-sponsored investigations, studies by groups of doctors, faculty sponsored investigations, and individual investigations. The college sponsored investigations deal with subjects which can be studied only in general practice, or studied there better than in hospitals or laboratories.

A measles investigation to assess the value of sulphonamides and antibiotics in preventing complications is already in progress, and has only been handicapped (the report remarks sadly) by the low incidence of measles in 1954. Better things are expected of 1955 and a report may be published by the end of the year. A national morbidity survey is being planned in collaboration with the Registrar-General's department; and a college records unit is being set up which should enable morbidity statistics to be recorded in a comparable way throughout the United Kingdom and overseas. Discussions with the Ministry of Health have resulted in the release of National Health Service records of dead patients to doctors needing them for research purposes. It has been suggested that clinical trials of therapeutic substances might be made by general practitioners, but this introduces some ethical problems to which the college is rightly giving serious thought. Finally the epidemic observation unit of the college has coöperated with the Public Health Laboratory Service in collecting specimens from suspected cases of influenza for identification of the virus. Through this unit one member of the college has already brought to light an outbreak of Q fever in the South West; and specimens from a recent outbreak of infective hepatitis in the South East have been collected and studied.

Among the study-groups, one is engaged in observing the clinical patterns of acute respiratory infections; another, interested in hereditary diseases, is examining the incidence of hypertrophic pyloric stenosis in the children of people who have themselves survived Rammstedt's operation; a third group is investigating the value of tonsillectomy; a fourth interested in psychosomatic disorders, is making a study of asthma and migraine; and a fifth small group is concerned with *asthma in children*.

Faculty-sponsored investigations include one into obstetrical work in South West England; a study of the symmetry of heads of babies in Northern Ireland to determine whether cranial asymmetry is related to right handedness or left-handedness; a study, in Yorkshire, of the course of cancer in patients who for one reason or another have not been treated; and an epidemiological survey in South East England of non-notifiable diseases including glandular fever, infective hepatitis, and epidemic winter vomiting.

These studies have been started with great enthusiasm but the college has it in mind, from the history of earlier collective investigations, that too great a dispersal of effort may lead to disappointment, and moreover (Professor MACKINTOSH notwithstanding) that there is a limit to the amount of voluntary work a family doctor can undertake over and above his practice. They are therefore wisely planning rather to consolidate the research work begun than to expand into new fields during the coming year.

It is interesting to compare this promising beginning with the research programme Professor MACKINTOSH foresees for general practitioners in years to come. The Public Health Laboratory Service, as he points out, has greatly added to their powers to contribute to systematic research; and he hopes that before long a more organised system of diagnostic centres will be developed and take the place of the health centres —"which are now by general consent slipping back into the waters of Lethe." These, like the Nuffield diagnostic centre at Corby,[3] would be staffed by technicians working under the supervision of specialists, and here general practitioners would have direct access to technical help in the more straightforward types of bacteriology, radiology, and pathology—or could, if they wished, undertake laboratory procedures themselves.

First in his list of possible studies Professor MACKINTOSH puts hereditary defects and diseases, for family doctors, and especially old established firms of doctors, have a better chance than most of noticing what happens from generation to generation. They can assess the significance of the eccentric relative and the slow child; can turn up records of stillbirths, neonatal deaths, minor congenital abnormalities, hæmophilia, Huntington's chorea, and pyloric stenosis; can observe the effects of common complaints on patients and their environment; and can assess the long-term effects of remedies old and new, and the protective value of vaccines. They alone have the chance of seeing the onset and full course of the diseases associated with old age, and can investigate both the basic and the precipitating causes of the so-called stress diseases They have remarkable opportunities, of which many of them make full use, of gaining skill in prognosis , and many a young doctor joining an old firm is startled out of his scientific calm by the uncanny skill of the senior partner in predicting the immediate and remote outcome of disease As Professor **MACKINTOSH** says, the true effects of pregnancy on chronic disease are largely unknown at specialist level Again, though the gross pathology of established disease can be seen and learned in hospital, the delicate innuendos of early disorder are to be apprehended only in general practice They are learned by watching the same patients for a lifetime Mental sickness, which sometimes has its origins in human relations, gives the general practitioner another field for study "The observation of years in a mental hospital or psychiatric clinic may not reveal as much about such *patients in their true* environment as the general practitioner learns in the course of his daily plodding ", and he it is, at present, who undertakes most of the follow-up and aftercare of patients who have been treated in mental hospitals Epidemiology still has many questions to be answered some incubation periods are still uncertain, and the modes of spread of many diseases are far from clear Professor **MACKINTOSH** notes the work in this field already being undertaken by the college, but mentions other possible inquiries—not only into the well-known infections such as chickenpox, herpes zoster, and *poliomyelitis, but into local non-infectious diseases* such as goitre and dental caries , and into chronic disorders such as rheumatism and bronchitis Finally, he suggests there is plenty still to study in the field of normal health and physiology—the disturbances of puberty and the menopause, the male climacteric, the onset of presbyopia, the significance of bodily and emotional types, and "the long fascinating story of child development "

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[1] Research in General Practice. Edinburgh: Royal College of Physicians. 1955. Pp. 88.

[2] Second Annual Report, 1954. Pp. 160.

[3] *Lancet* 1954 i 871

So much for the programme but there are, he hints, obstacles The first is the medical curriculum, which not only fails to prepare the student for research under the conditions of medical practice but introduces him mainly to the late stages of disease, gives him the scantiest notions of the relations of sickness to social and industrial life, and does not equip him with enough elementary statistics to conduct simple investigations in the field of general practice Given an early understanding of statistical methods and of the importance of controls he would quickly recognise how little is other apparatus needed for important work two eyes, a pen, and a record card often suffice Other obstacles are the want of liaison between general practitioners and consultants, the scarcity of leisure, the broken time, the prejudice of patients ("people in general have a respect almost amounting to awe for research, but they do not enjoy being the subjects of investigation themselves "), and the absence of a stimulating atmosphere, such as is found in hospital or laboratory But all these obstacles, he urges, can be overcome The college is already playing its proper part by giving help and guidance (particularly in the matter of collecting accurate statistics), by organising research teams and groups, and by keeping keen people [illegible] with one another and with experts in their subjects . Other incentives must come from elsewhere—from the medical schools, which must equip their students better for research , from the Ministry of Health, which can distribute information about minor disorders (bronchitis, common colds, and the neuroses) which are responsible for much ill health, and as a by-product from group practice which gives the doctor time for reading, writing attending *clinical meetings, looking* after his own health , and developing more fully his skill in his profession

Cell Type in Bronchial Carcinoma

NO-ONE would suggest that surgery is an adequate weapon in the treatment of bronchial carcinoma, but it is the best we have , and with modern technique roughly one quarter to one third of patients who have "*curative*" resections survive operation by at least five years $^{1-6}$ *It* is now clear that the prognosis in these cases is greatly influenced by the cell type of the tumour $^{5-8}$ Bronchial carcinoma is usually classified histologically as squamous cell, adenocarcinoma, or undifferentiated , but **KIRKLIN** et al ^{6} consider that it is worth subdividing the undifferentiated group into *small cell* carcinoma and large cell *carcinoma* The *cells in small cell carcinoma* have little cytoplasm, *they are irregularly arranged,* and as the nuclei are often spindle shaped the term "oat cell " is commonly applied to this group The cells in **KIRKLIN**'s large-cell type have more cytoplasm, but the other histological features are variable, sometimes resembling those of the small cell variety *and sometimes those of the squamous cell type,* so *that pathologists recognising only three groups* would put them in one or other of these categories

The prognosis in the small-cell (oat-cell) type is very poor, though occasional good results are achieved On the other hand, the outlook in the squamous cell variety is relatively good $^{5-8}$ There is more doubt about the prospects with an adenocarcinoma, **KIRKLIN** and his colleagues,[6] for example, consider that the chances of a successful operation are almost as good as with a squamous cell tumour, whereas **HOLMES SELLORS**'s experience ^{5} has been that the chances are not much better than in the deadly small cell group The prognosis in the large cell variety is poor, though *it* is apparently *somewhat* better than when the tumour is of the small cell type [4] Moreover, squamous-cell carcinoma means more than a better chance of survival after a "curative" operation, for a higher proportion of such growths are amenable to surgery when first diagnosed $^{6\ 8}$, so that at first sight it seems fortunate that in most analyses of the results of treatment in bronchial carcinoma this variety is commonest But, as **BIGNALL** has lately pointed out,[9] it is the highly malignant small cell

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1 Churchill E D Sweet R H , Soutter L Scannell, J G *J thorac Surg* 1950, 20, 349
2 Ochsner, A De Camp P T De Bakey M. E Ray, C J *J Amer med Ass* 1952, 148 691
3 Gibbon, J H jun , Allbritten F F jun Templeton, J Y Nealon T F jun *Ann Surg* 1953 138, 489
4 Boyd, D P , Smedal, M. I Kirtland, H B jun , Keller, G E Trump, J G *J thorac Surg* 1954, 28, 392
5 Sellors T H *Brit med J* 1955 i, 445
6 Kirklin J W , McDonald, J R , Clagett O T Moersch H J Gage R P *Surg Gynec Obstet* 1955 100, 429
7 McDonald J R , McBurney, R P Carlisle J C , Patton M E *J thorac Surg* 1951, 22 62
8 Ehler A , Stranahan, A Olson K B *New Engl J Med* 1954 251 207
9 Bignall, J R *Lancet*, April 16, 1955 p 786

tumour which preponderates in necropsy studies, and this discrepancy may be explained by the fact that it is the potentially operable cases which go to the special centres from which statistics of survival rates usually come

It is difficult to get reliable information about the actual proportion of all cases which are suitable for surgery when first diagnosed but it is safe to say that it is depressingly low Can the position be improved? Nothing can be done about the most decisive factor influencing survival—the cell type of the tumour—but there is a chance to reduce the delay between the appearance of symptoms and diagnosis Even so, it is doubtful whether any sizeable improvement in the situation would follow and experience so far suggests that mass radiography [9,10] has no striking contribution to make towards a reduction in mortality Indeed BIGNALL came to the sombre conclusion that, even with the most efficient medical service possible we could not, with present methods of diagnosis and treatment hope for any substantial improvement He suggests that we should aim at more effective palliative remedies and it is only necessary to consider the vast sum of human suffering involved to appreciate the value of any such advances

A Century of Army Pathology

THE story of pathology in the Army is one of small beginnings, big opportunities distinguished achievements, and heavy responsibilities faithfully discharged At the centenary of the service last week there was no lack of great names to honour or fine work to recall but above all there was a sense of this work continuing Nor is it limited or separate from work elsewhere Nowhere more than in pathology is there interchange between Army and civilian medicine, and the mixed gathering at the Royal Army Medical Corps Headquarter Mess on April 27 was evidence of a symbiosis which has been particularly happy and always beneficial

The day was chosen because it was on April 27 1855 that Dr R S D LYONS, an Irish physician, and his "two able assistants" Dr WILLIAM AITKEN and Dr DOYLE, were sent their instructions on the pathological researches they were to undertake at Scutari among the sick and wounded of the Crimea In his centenary article on the service Major-General SACHS [11] quotes these instructions

> 4 As Morbid Anatomy is of little value unless studied in connection with the history of the disease you and your Assistants will require to visit the Hospital wards in order to become acquainted with the symptoms and characters of the diseases during their progress but you will not interfere with the treatment of the patients. In making notes of the cases, the name of the patient, and the number of his regiment should always be stated as by this means the nature of his duties, and the place where he was first attacked by disease can be more easily ascertained
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> 6 It is expected that you will not content yourself with the simple dissection of the subject and the demonstration of the morbid parts, but that you will submit them to microscopical examination

Even at this early date in an era when little was known about the staining of tissues the importance of the microscope is usefully emphasised, and the instructions are well drawn. Less understanding was shown by the War Office when for years it blocked the plans made by FLORENCE NIGHTINGALE for a school of military hygiene and when at last, in August, 1860, the Practical Army Medical School was opened at Chatham the first 10 students found bare walls and no equipment Nevertheless it was not long before the school as the Army Medical College at Netley, redeemed its bad start Its professor of pathology from 1860 to 1892, Sir WILLIAM AITKEN F.R.S., became the father of military pathology and was to make considerable contributions to medicine through his pupils Thus the roll of his assistant professors includes Surgeon Major TIMOTHY LEWIS (F.R.S.-elect when he died at 45) Sir DAVID BRUCE F.R.S and Sir DAVID SEMPLE. He was succeeded by Sir ALMROTH WRIGHT, F.R.S who in 1903 when the college came from Netley to London was in turn succeeded by Sir WILLIAM LEISHMAN F.R.S In 1914 and again from 1919 to 1921 the chair was held by Colonel S LYLE CUMMINS

In the decade preceding the first world war the value to the Army of a well organised pathology service was gradually recognised, and the training of regular Army pathologists proceeded steadily, with research by teams as well as individuals The war saw the development of mobile bacteriological laboratories, hospital laboratories and research laboratories and classical work was done on wound sepsis tetanus, gas gangrene shock, and many forms of infectious disease The war also showed the need for a degree of central direction of all these vital undertakings, and in 1919 the Pathology Directorate was founded at the War Office with LEISHMAN as first director assisted by DAVID HARVEY and A C H GRAY At the same time the Army Pathology Advisory Committee came into being—a body to which Sir FREDERICK HARRIS *director general of Army Medical Services* paid a special tribute last week. (Among its original members was Dr MERVYN GORDON F.R.S who attended every one of the seventy meetings during his lifetime) Under these arrangements development continued and research flourished especially in the 30s In India the pathology service profited greatly from the energy and drive of Major (now Major General) JOHN MANIFOLD Also in India, J S K. BOYD F.R.S, made his observations on dysentery bacilli, and L T POOLE worked with H E SHORTT of the I.M.S on the virus of sandfly fever At the Royal Army Medical College MARRIAN PERRY was collaborating with H. T FINDLAY and H J BENSTED on virulent typhoid strains in the production of vaccines and BOYD investigated the dosage and administration of tetanus toxoid

In 1939 the Army had a well developed and efficient pathological service capable of rapid expansion Under the directorship of Major General PERRY, the formation of an Army Blood Transfusion Service was undertaken by Sir LIONEL WHITBY who with such lieutenants as G A H BUTTLE W D'A. MAYCOCK, and G T L ARCHER made it one of the outstanding achievements of medicine in the war In 1941 Major General POOLE succeeding PERRY as director of pathology, took over a task now made immensely intricate by the requirements of large forces in widely separate theatres of war and by the need to arrange and assist many kinds of urgent research by

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[10] Boucot K R, Sokoloff M J *Amer Rev Tuberc* 1954 69 161

[11] Sachs A *J R Army Med Cps* 1955 101 100

many different kinds of group How well that task was performed, by him and his assistant Lieut.-Colonel **BENSTED**, is known to many colleagues in all departments of medicine, who were thankful for his combination of high standards with a receptive mind and readiness to help After his retirement in 1945, the directorship was filled, for shorter periods, by Brigadier **BOYD**, by Brigadier **FINDLAY**, and by Major-General **SACHS**, from whose lecture at the college on April 27 we have drawn many of the facts of this outline Since 1953 the director has been Brigadier **ARCHER**, who arranged this memorable commemoration and at last week's dinner gave what he called the primary response to the toast of the Army Pathology Service proposed by Sir **LIONEL WHITBY** This is a toast with which a great many people have reason to associate themselves—even though they may never have heard of the service

Annotations

POLIOMYELITIS VACCINATION

MISGIVINGS about the new poliomyelitis vaccine,[1] lately put into extensive use in the United States, have been aggravated by last week's news that a number of children have fallen ill with paralytic poliomyelitis shortly after vaccination It is reported that 35 children have had paralytic poliomyelitis within a short time of vaccination,[2] and 2 have died Almost all these children had been injected with vaccine prepared by the Cutter Laboratories, of Berkeley, California, and supplies from this manufacturer have been recalled In the States of Idaho and California the immunisation programme has been stopped for the time being In Washington the situation has been examined by a group of advisers, including Dr Salk, and they have recommended that inoculations should continue[3] About 4 million people, nearly all children, have so far had a first injection In this country the Medical Research Council decided on Monday that their trials would not start until fuller reports of the American results were available

There are three possible explanations of what has happened First, the children may have been going to get poliomyelitis anyway, and vaccination was too late to have any preventive action Second, the children may have been carriers of poliomyelitis virus, and vaccination acted as a provoking stimulus in a similar way to pertussis and diphtheria immunisation Third, the vaccine may have contained live virus At present there is not enough evidence to decide which explanation is correct, but the third seems the most likely As there is nothing definite to suggest that vaccine manufactured by other laboratories is liable to produce paralytic poliomyelitis, it may be that the virus in certain batches of the Cutter vaccine had been incompletely inactivated

If it should turn out that the vaccine contained live virus two important questions must be considered. Did the Cutter laboratories follow closely the technique of inactivation by formaldehyde recommended by Salk ? It seems unlikely that any firm would knowingly vary the procedure, and if these methods were in fact closely followed the margin of safety of this technique should be re examined In particular, there should be a thorough scrutiny, in a number of different laboratories, of the kinetics of inactivation of all three types of poliomyelitis virus by formaldehyde under various conditions The second question concerns the tests of safety which were applied to this particular vaccine Previously, vaccine had been tested to exclude the presence of live virus by tissue-culture techniques and by intracerebral inoculation of monkeys If the tests carried out on the suspect vaccine were not as rigorous as those applied during last year's vaccination trial, the remedy seems clear Many thousands of children received the Cutter vaccine, so the relatively small number of cases of paralytic poliomyelitis may mean that only a few infective virus particles remained in the vaccine On the other hand, if the vaccine passes the safety tests but is still suspect on the grounds of a statistical analysis of the incidence of poliomyelitis following its use, then we must think again about the safety tests Is it wise to apply the results of tests with scores of monkeys to the vaccination of hundreds of thousands of children? We hope that it will not be necessary to make these further inquiries, and that the postvaccination cases may turn out to be unrelated to the vaccine But at the moment it seems unlikely that the vaccine will escape all blame

ANÆSTHESIA IN OBSTETRICS

THE advances in anæsthesia in the past few years have usually been accompanied by administrative steps which have made the new techniques available to almost every patient who has to have an operation in this country But this scarcely applies to anæsthesia in obstetrics, and there are good reasons to reconsider the position in this branch of anæsthesia, as was done at a meeting of the section of obstetrics and gynæcology of the Royal Society of Medicine on April 22

There has been some uneasiness about an apparent increase in maternal deaths due to anæsthesia, but this may well be only a relative increase, brought about by a fall in the number of deaths from other causes One danger lies in giving general anæsthesia to a patient who has not been properly prepared for it, the mother is sometimes given food and drink almost up to the last moment, and there is occasionally, after prolonged labour, a gastric atony and a stomach full of fluid, which can remind the anæsthetist of paralytic ileus or intestinal obstruction Again, these anæsthetics are not always given by those thoroughly familiar with the drugs they are using, or with the particular points on which to concentrate during the administration Whenever anæsthetics are given to mothers in labour, suction apparatus should be close by, and the delivery table should be one which will tip both head up and head down The head-up position, with the use of a relaxant drug and the passage of a cuffed endotracheal tube, is perhaps the safest method in experienced hands Sometimes induction at least should be carried out in the lateral position

The dangers of general anæsthesia emphasise the case for local or regional analgesia whenever possible General anæsthetics are essential from time to time, for intra-uterine manipulations such as internal version and manual removal of a retained placenta, but these occasions could perhaps be chosen more carefully General anæsthesia is often adopted without question because it allows every conceivable procedure to be carried out but in many cases another and safer method might have been equally effective Local and regional blocks have difficulties and dangers of their own, but there are many impressive reports of series in which they have been successfully used Perineal field block is probably the safest for mother and baby properly carried out it will permit low, possibly mid-cavity, forceps delivery and it is particularly suitable for breech delivery As for domiciliary operations, modern antenatal care has made a high proportion of them straightforward, but the same dangers can threaten At the meeting at the Royal Society of Medicine last month, Dr R B Parker gave statistics from Birmingham which showed that the rate of maternal anæsthetic death was greater in hospital actice than in domiciliary obstetrics The domiciliary næsthetic is almost always chloroform, with or without her The dangers of chloroform are well known and s use is sharply condemned on all sides; but many ill mourn the passing of chloroform from hospital ractice, and miss the smooth induction and the exibility it affords At present there is nothing which uite replaces it for those who give most of the anæs hetics in hospital obstetrics

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[1] *Lancet* April 23 1955 p 851
[2] *New York Times* May 1, 1955
[3] *Times* May 2 1955

It seems that there is much useful information to be btained from a wide survey of anæsthetic mortality nd morbidity in obstetrics, both domiciliary and nstitutional This should take into account the circumstances of the operation the equipment available (such s tipping bed and suction apparatus) and the experience nd training of the anæsthetist

XERORADIOGRAPHY

Is a new form of X ray photography xeroradiography o wet chemicals are used to develop the latent photo aphic image The process is a photo electric one and as first described by Carlson in 1937 Although it has een in use in commercial photography for some time, edical applications are only now being investigated. he technique depends on the property of a group of ubstances, known as semi-conductors, to hold an elec tical charge in the dark but to allow it to leak away when xposed to light or X rays Of these substances the ost promising so far investigated is amorphous selenium xerographic plate consists of a metal base on which is posited a layer of selenium 120–150 µ thick. It is otected from light and mechanical damage by a cover milar to an ordinary photographic cassette Before e the plate is charged in a special chamber by a high ltage D.C. source, which gives the selenium a positive ectrostatic charge The plate is exposed in the normal ay and the image is developed by spraying a fine wder on the surface of the plate in another light oof chamber The powder is taken up by the surface the plate according to the amount of charge remaining d so an image appears It takes about 10 seconds to arge the plate and about 20 seconds to powder it diographically speaking these times are remarkably rt even compared with those possible by the rapid t processing methods now available and there is the ded advantage that no dark room is required. Indeed whole charging and powdering equipment can be ilt into a trolley 4 ft by 2 ft or less and tucked into any rner of the X ray room or operating theatre Costs problematical but the charging and powdering achine may cost from £200 to £500 and the plates about each and since these can be re used indefinitely the ethod offers a cheerful prospect of reducing costs

The quality of the image is a more debatable point. The rograph is rather like an etching in black and white d it is viewed by reflected light To the unaccustomed e at least it is more difficult to interpret than e conventional radiograph. The image is of low ntrast, and soft tissue and bones are easily distinguishable on the same plate The powder tends to build up lines along the margins of the more dense parts of the age and this enhances the contrast and the clarity detail Fine wire grids as close as 1200 to the inch can resolved whereas, with normal film detail deteriorates 180 lines per inch[1] At the present stage of develop ent the speed of the xerograph is not all it might be ing about the same as that of non screen film; posures are therefore unacceptably long for the heavier rts of the body Another disadvantage is that a rmanent record can be made only by photographing e xerograph on miniature film or by copying it electrically; this would be a particular drawback when a ries of radiographs has to be inspected regularly or hen it is likely that one or more films will be needed for future reference Further research into the possibility of using a translucent base, to allow inspection by transmitted light, and of reducing the exposure required may make the method more useful medically

Much of the work on xeroradiography has been done in this country by W D Oliphant in Edinburgh, and trials of the equipment are well under way From America it is depressing to learn that the method is being considered as a means of replacing stocks of ordinary film fogged by atomic explosions But more cheerful news of the interesting medical possibilities should be coming shortly

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[1] Roach, J F Hilleboe H E J Amer med Ass 1955 157 899

SECOND AID

THE treatment of an injury begins almost as soon as it is sustained The patient himself—or a witness who renders assistance or tenders advice—is his first "doctor" From this haphazard beginning he passes through the hands of successively more experienced helpers until he undergoes definitive treatment His progress may involve a parent an older workmate, a resourceful bystander, a civilian or policeman trained in first-aid, the chemist,' a nurse, a doctor a hospital and perhaps ultimately a specialist in traumatic surgery or a team of specialists The more serious his injury the more likely he is to follow this sequence to its end but how far he travels along the line depends also partly on chance and partly on the organisation Many of those who get no further than one of the early stages might have profited if they had been carried at least one stage further There is still much avoidable disability because patients with trivial injuries are not brought to clinics and services which are there to treat them until some complication has set in Of those sent to hospitals well fitted to deal with them some have suffered by delay in the preliminary "filtering some by well meaning but unenlightened handling on the way, and some because no one appreciated that a patient with a dangerous condition may not look dangerously ill

One particular section of this line is receiving increasing attention, as is well illustrated by two publications from the committee on trauma of the American College of Surgeons[1][2] One is the fifth edition of a monograph on the treatment of fractures the other a new companion to it is a similar work on the early care of soft tissue injuries The growing realisation of the importance of this second type of injury is reflected in the size of the monograph on it, which is twice that of the other Both combine simplicity brevity and absence of distracting controversy with remarkable comprehensiveness. Both may be accepted as a concise presentation of the most authoritative views in contemporary American teaching Both emphasise the value—often the *supreme* value—of correct *early* treatment which may lie in the hands of younger and comparatively inexperienced people They are aimed at interns and residents in the hospital who serve their periods in the emergency room" and at all doctors who have to do with the treatment of injuries but there is sufficient indication of the later specialised treatment for readers to understand why initial decisions have a vital influence on the final result

It is neither possible nor desirable for every minor injury to be submitted to highly specialised services. Nevertheless much delay in recovery may be avoided if those responsible for early care are guided to select accurately the more serious injuries and if they are briefed on the best way to deal with these before they are sent on Senior surgeons cannot sit all day in their casualty departments waiting for the next accident but they can make clear their wishes on early treatment and they can inform their juniors of the type of surgery likely to be required later in the day House-surgeons casualty officers, and "interns" usually have a comparatively brief term of office Many casualty departments and accident rooms have a periodicity in the standard of their service which corresponds with the length of the doctor's appointment Continuity of policy among successive holders is difficult to maintain, and these publications could do much to maintain it

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[1] An Outline of the Treatment of Fractures By the Committee on Trauma American College of Surgeons 40 East Erie Street, Chicago 11 Ill., U.S.A 1954.

[2] Early Care of Soft Tissue Injuries By the Committee on Trauma, American College of Surgeons 1954

ANTI-HISTAMINES AS HYPNOTICS

MANY anti histamine drugs in common use cause drowsiness, and that is usually unwelcome, but Straus et al,[1] in New York, have tried to decide whether this property can be turned to good account In a controlled experiment they have shown that the anti histamine, methapyrilene hydrochloride, in a dose of 50 mg by mouth, is as effective a hypnotic as 100 mg (gr 1½) of phenobarbitone This work confirms a general clinical impression, but anti-histamine drugs are unlikely to be widely accepted as alternative hypnotics to barbiturates

The experiment is of interest because of the methods employed in evaluating methapyrilene's hypnotic powers It was conducted on the "double-blind" principle, and methapyrilene was compared with a positive control (in this case phenobarbitone) and with a negative control (an inert capsule) The "cross over" technique was used—that is, all patients received all the substances being tested, but different sequences were followed in the various patients The choice of phenobarbitone as a positive control was perhaps unfortunate, for this drug is usually classed as a sedative rather than a hypnotic, and 200 mg (gr 3) of pentobarbitone would perhaps have been a better dose The greatest difficulty in an experiment of this kind is the selection of suitable patients Ideally (for unquestionable results), no one should sleep well after the placebo and all should sleep well after the positive control As the experiment was designed with an evaluation period of three weeks, it was necessary to select patients with chronic insomnia relatively uninfluenced by factors other than the change of medication Obviously the ideal conditions will rarely be obtained in practice, and, in fact, although Straus et al selected their 54 subjects with great care (only male patients were included), 30% showed an excellent response to the placebo The number of variables might have been less if each drug had been given only once to each patient, and if a larger number of patients had been used

The criteria of a night's sleep were the patients' own statements in a standard interview and the observations of a night nurse who shone a flashlight on each patient regularly during the night The nurse's impression of the patient's sleep was consistently better than that of the patient himself Other methods of measuring sleep, notably electro encephalography, were considered but all were rejected as inferior to the simpler tests employed Each night's sleep was classified and scored, and the data so obtained were statistically analysed in considerable detail The conclusion was that, as a hypnotic, methapyrilene was superior to the placebo and about equal to phenobarbitone The refinement of the statistical methods seems scarcely suited to the analysis of data measured on an arbitrary scale, and in the presence of many uncontrolled and often unidentifiable variables But Straus and his colleagues have given a very good example of a carefully designed experiment, and it would be a great advance if all new hypnotics were examined with equal care On the other hand, some may think that the information obtained by an elaborate study like this still falls short of scientific proof, and that the judgment of an experienced clinician, based on the observation of relatively few patients (and perhaps of himself on the night train to Scotland), is still a very good measure of what a hypnotic is really worth

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1 Straus [illegible] Eisenberg J Gennis, J *Ann intern Med* 1955 42 [illegible]

ORTHOSTATIC PROTEINURIA

ORTHOSTATIC proteinuria is a condition in which th urine is normal while the patient is lying down, b contains protein when he is up and about It is usual considered to be a temporary and harmless anomal King,[1] in a study of 4000 cases of proteinuria in th United States army, has put forward the view that i is often permanent and not completely benign Th proteinuria persisted for three years in 131 of 170 case and many of these gave a history of proteinuria for u to ten years previously These observations agree wi those of Thorp and Wakefield[2] who found that 43 o 64 patients still had proteinuria after six years Th incidence of anatomical abnormalities of the kidneys an ureters in cases of orthostatic proteinuria is unusual high King found that 18 of 56 cases showed radi logical abnormalities by intravenous pyelography, an Young et al[3] have reported a similar proportion

The amount of protein lost in the urine may occasi ally be as great as in severe glomerulonephritis. Co centrations of protein as high as 4 g per 100 ml in sing urine specimens have been reported,[4] and Wolman states that the range of concentration in 24 hour spe mens is 15–545 mg per 100 ml, with a mean value o 74 mg per 100 ml The highest level corresponds to protein loss of about 8 g daily, equalling that found many examples of the nephrotic syndrome Electr phoresis showed that the proportion of globulin w unusually high[1]

There is still controversy about the cause of th condition Sonne[6] considered it was the result of co pression of the left renal vein as it crossed the abdomi aorta, and Bull[7] thought that rotation of the liv during lordosis compressed the inferior vena cava an so increased caval venous pressure King believes th further experimental evidence is necessary before eith of these hypotheses can be accepted King and Baldw have confirmed Bull's finding[7] that there is a profou fall in glomerular filtration rate and renal plasma fl in the erect lordotic posture, but they found no signific difference in filtration rate or plasma flow when ca of orthostatic proteinuria were compared with n proteinuric controls

The immediate prognosis in cases of ortho proteinuria is good, and it is certain that this anom does not indicate rapidly progressive renal dise Insurance statistics suggest, however, that the morta over many years is significantly greater than in cont "good life" cases Daley[9] states that actuarial statis published in 1938 showed a mortality in 52,000 case "intermittent" proteinuria of 128% of the expec level Further experience[1] up to 1951 suggests t the mortality rises to 150% of the expected figure that the extra deaths are most commonly due cardiovascular disease

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THE next session of the General Medical Council open on Tuesday, May 24, at 2 P M, when Sir Da CAMPBELL, the president, will deliver an address. T Medical Disciplinary Committee will meet on Thursd May 26, at 10 30 A M

Prof G W CORNER of Baltimore has been elected foreign member of the Royal Society in recognition his work on the endocrine control of gestation especially on the function of the corpus luteum mammals

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1 King S E *Ann intern Med* 1955 42 296
2 Thorp, E G, Wakefield F G *Ibid* 1933 6 1565
3 Young H H, Haines, J S Prince, C L *Milit Surg* 1
92 353
4 Hopper J Bolomey A, Wennesland R *Ann intern*
1954 41 18
5 Wolman I J *Amer J med Sci* 1945, 210, 86
6 Sonne C *Z klin Med* 1921 90 1
7 Bull G M *Clin Sci* 1948, 7 77
8 King, S E, Baldwin, D S *Proc Soc exp Biol* N Y 19
86 634
9 Daley R M *Urol cutan Rev* 1942, 46, 13

Special Articles

CANCER

THE PSYCHOLOGICAL DISEASE

MALCOLM DONALDSON
F R C S F R C O G
DIRECTOR OF CANCER SURVEY YORKSHIRE COUNCIL, BRITISH EMPIRE CANCER CAMPAIGN

THE title of this article is not intended to suggest that cancer is a ' psychosomatic ' disease but rather to point out that besides the physical disease of cancer there is a psychological condition of cancer apprehension,' which affects almost the whole population This mental attitude is present in many members of the medical profession although in their case it assumes a rather different form and the fact that discussions on cancer education often generate more heat than arguments about politics or even religion, may in itself be additional proof of my thesis.

PREVALENCE

Is this apprehension of direct harm to the community ? Clearly in its acute form of cancerphobia ' it causes great harm to some individuals and each year a few suicides are recorded, where the unfortunate victim is found to be without trace of the disease Mental worry even if only intermittent as is often the case in cancer apprehension must also be harmful to the individual, and, if widespread, must surely be bad for the community What evidence is there that cancer apprehension is widespread ? There is no statistical evidence but surveys in America are suggestive and a survey among 1200 Manchester women[1] showed that three-quarters considered it the most alarming of all diseases

Every doctor has patients who visit him with vague symptoms, and if at the end of an examination the doctor says I am glad to say that I can find nothing serious, no evidence of tumour or cancer ' as often as not the patient will say Thank God, that was what I was really worried about " Such cases clearly indicate the presence of cancer apprehension Unfortunately some of these cancer-apprehensive patients are not recognised they are labelled neurotics or neurasthenics and they continue to live on the doctor s doorstep in the hope of being reassured

Reluctance in the dislike to mention the word cancer is also evidence of apprehension Obituary notices refer to a ' long and painful illness bravely borne (Heart-disease with its greater mortality is never mentioned in this way) Doctors even if they are not anxious about themselves are anxious that nobody should hear or think about cancer Whether a patient should be told the truth must depend on circumstances. Often the relatives are told but the patient deceived—if he or she can be deceived which is doubtful Later if the relatives think they have cancer the doctor finds it hard to convince them that there is no cancer In the Manchester survey already mentioned 40% of the women thought that the patient should be told Any attempt to keep the disease ' hush hush ' must fail because it is met with so frequently Each year in this country about half a million are added to the number of people who have already come in direct contact with a patient

An incident illustrating the fatalistic and defeatist attitude of some doctors towards cancer happened to me When I entered hospital to be investigated for a possible gastric carcinoma one of my colleagues said Of course you know you have not got a carcinoma you would never go into hospital On leaving hospital after an exploratory laparotomy which fortunately proved negative another colleague said ' Of course you were the only person who thought it might be carcinoma Would these remarks have been made about any other disease ?

Though there may be a difference in opinion as to how widespread is cancer apprehension there is no doubt that it often delays diagnosis There are no figures to show how many patients put off a visit to the doctor for fear that the condition may be cancer but the answers given in the Manchester survey to the question why women are more frightened of getting cancer than any other disease, are probably also the reasons for delay in reporting symptoms to a doctor Of these the answers that it is fatal ' ' incurable ' ' gets worse " only know when it is too late,' and " because of the pain and suffering " head the list

There are figures, however which show the time that elapses after a patient has noticed a symptom before he or she seeks advice Stocks[2] reported that the median number of months interval between the earliest symptom and the start of treatment for cancer of the uterus was 5 7 months (taken from the figures supplied by twenty six hospitals), for the breast 6 months and for the rectum 5 6 months Figures collected by the Yorkshire council of the British Empire Cancer Campaign show much the same delay

TREATMENT

What can be done to lessen apprehension and thus obtain earlier diagnosis ? Surely the answer can only be to educate the public by giving information about the accessible cancers and by encouraging people to talk about cancer, and thus to bring their fear to the surface and to face it Those who oppose this plan do so chiefly on the grounds that attempts to educate the public will increase cancer apprehension and fear If true this would certainly defeat the object of obtaining earlier diagnosis Psychiatrists could help us to settle this question, but unfortunately, though interested in the treatment of true cancerphobia patients they have little time to study the problem.

The Yorkshire Council of the B E C C, with the help of some of the local health authorities in the area, have lately given 220 lectures to the public on cancer education At the end of most of these a printed slip is passed to each member of the audience asking whether the lecture has increased their worry and such lectures should not be given or whether it has diminished their worry and more lectures should be given The results from 5740 votes shows 99 1% in favour 0·2% against while 0·7% put a question mark

The other argument used against cancer education is that even if patients are persuaded to visit their doctor when a symptom is noticed the number of cancers treated in the early stage will not be greatly increased because of the large number of growths that disseminate before giving rise to symptoms It is very doubtful *whether this is true* of the accessible cancers which are the only ones that cancer education can hope to benefit

Figures quoted in support of this are usually based on the results of treatment within six months of noticing symptoms and after six months This is, in fact a *comparison between two different types of growth* The first set of figures includes all the rapidly growing tumours as well as the slow growing well-differentiated tumours whereas the second set includes only *the well* differentiated, slow growing ones The figures needed are those for 0–1 month 1–2 months 2–3 months &c., for the accessible cancers In the Manchester survey 76% agreed that there should be freer public discussion of the symptoms

If the psychiatrists could confirm the psychological benefit of cancer education it would be a great help to those of us who are trying to obtain earlier diagnosis

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[1] Paterson R., Aitken-Swan, J *Lancet* 1954 ii 857

[2] Stocks P Studies on Medical and Population Subject No
H.M. Stationery Office 1950

WORK OF A GERIATRIC UNIT

A SURVEY OF 13,500 PATIENTS

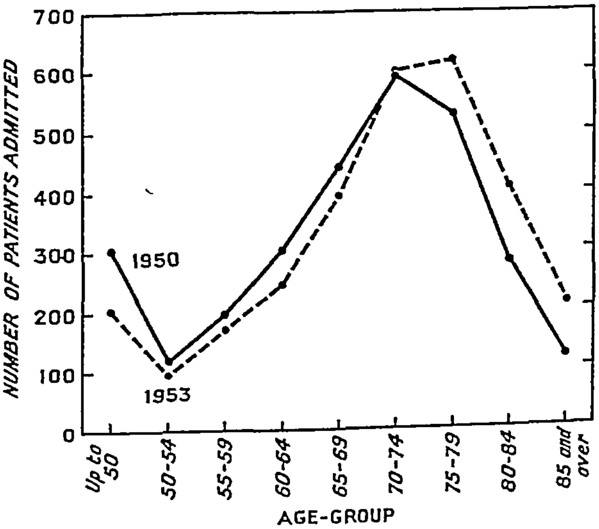
KENNETH B GIBSON
M.B E , M D Lpool, M.R C P
LATE PHYSICIAN SUPERINTENDENT, NEWSHAM GENERAL HOSPITAL, LIVERPOOL

I HAVE recently completed a survey of all inpatients treated in the 18 medical geriatric wards of this hospital, from the beginning of 1950 to the end of June, 1954 Of these 13,500 patients, 11,000 were over sixty years of age, and some of the findings seem likely to interest others concerned with planning hospital care for the elderly

The Background

Newsham, like many of the country's larger hospitals, had a humble origin as a 19th-century poor-law institution As time went on, buildings designed as dormitories for the able-bodied gradually came to be used as wards for the growing number of infirm inmates The occupants of these wards were mostly old and bedfast Some were merely frail and homeless, some were disabled by chronic disease, some were acutely ill For several decades there were few facilities for medical investigation, treatment, or rehabilitation , but a high standard of nursing care, provided by a hard-working though largely untrained staff, tended to conceal the defects of the system These defects were aggravated and became more conspicuous during the second world war, when a depleted staff had to meet the additional demands of the Emergency Medical Service Its new rôle as an emergency hospital led to the appointment of its first two resident medical officers, but the war precluded any large scale improvement

In 1946 there began a phase of development which has continued ever since, with a minimum of interruption due to the change of management in 1948 Staff was augmented , equipment was provided , and, despite financial restrictions and material shortages, some modest but useful structural alterations have been achieved The original programme for the modernisation of the hospital's 34 wards is now nearly complete, and ancillary services have been steadily expanded to meet the increasing demand for investigation and rehabilitation of a medical staff which now numbers 36 At the beginning of the period of this survey there were already adequate facilities for radiology, pathology, physiotherapy, and occupational therapy , and an almoner's department dealt with social problems By the end, all these departments had been further improved and ma new ventures had been started—e g , there was a chirop dist, a dispensing optician, and a cardiographer, t hospital had its first operating-theatre , and a sm follow-up clinic had been set going



of the ages of patients admitted in 1950 and 1953.

The number of beds in medical geriatric wards inev ably fluctuated during four and a half years, and t over all result was a slight reduction from about 740 in 1950 to 707 in 1954 For instance, 16 beds were lo when part of a male ward was converted to enlarge th X-ray department , others were sacrificed to mu needed sanitary improvements in several wards In t review I have excluded 2 wards for senile dement a 1 mixed psychiatric ward Also I have ignored int departmental transfers , but this two way traffic is to small to influence the main findings

Most of the patients in the survey were admitted a the request of their own general practitioners Durin the greater part of each year there is a waiting list, a patients are admitted in their turn unless their doct ask for priority Apart from an occasional need to a the relative urgency of claims for priority, there was n selection or screening of admissions by the hospita medical staff About 9–10% of each year's admiss were transfers from hostels and other hospitals

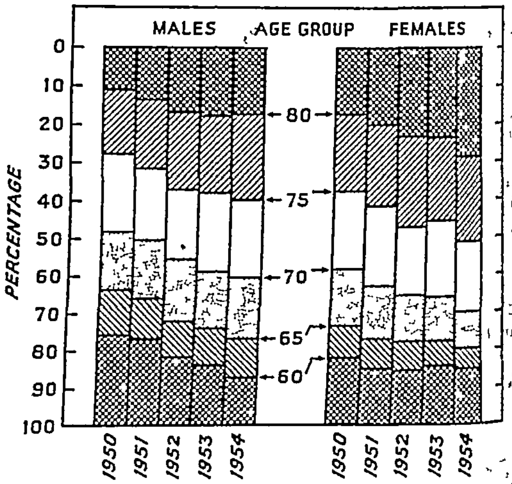


Fig 2—The changing age-distribution of men and women admit geriatric wards in 1950–54 (1954 percentages based on adm during the first six months of the year)

The 18 wards included in the survey form a compo geriatric unit, which undertakes not only investigat treatment, and rehabilitation, but also the long te care of patients with chronic disease who cannot adequately nursed outside hospital The latter are segregrated in a separate annexe In general, a wa or group of wards, retains its own long stay patie but tends to concentrate them as a matter of convenie This system is largely dictated by local conditions offers many advantages Both medical and nursing share the variety and interest of different types of w and most elderly patients like to remain with the staff throughout their stay Moreover, the atmosph of an active ward helps to sustain an expectatio ultimate discharge in the minds both of patients their relatives

Analysis of Results

Age of Patients

Patients over seventy years age of increased f 1516 (52 8% of all admissions) in 1950 to 1822 (6 in 1953, and represented 65 2% of all patients adm in the first six months of 1954 Higher in the age-sc the proportion of admissions over eighty years of increased from 13 9% in 1950 to 23 2% in 1953 (fig 1

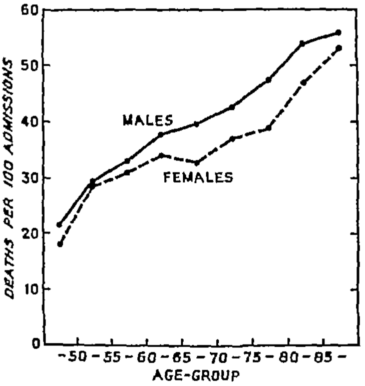


Fig. 3—Mortality of whole series at different ages.

Like other geriatric units (Thomson 1949 Morton 1952 Amulree et al. 1952 Andrews and Wilson 1953) we found that men tend to be admitted at an earlier age than women (fig 2) In both sexes the age on admission rose in successive years, but women showed a greater increase than men The increasing proportion of men in the older age groups depended partly on a reduction in the proportion under sixty years of age while the numbers of women under sixty varied very little

Mortality

As in the general population, mortality increased with age after fifty years and in every age group women had a lower mortality than men (fig 3) Death rates per 100 admissions varied from 18·0 (women under fifty) to 55·4 (men aged eighty five and over) the death rate did not pass the 50% level until age eighty for men and eighty five for women

Despite the increasing age of patients admitted mortality rates fell during 1950–53 Annual rates per 100 admissions (table I) are convenient for comparison though not all the patients dying in a given year were admitted in that year The mortality of both sexes combined shows a fall in each year after 1950 with the exception of 1951 (This interruption of the downward trend seems to have been caused by a severe influenza epidemic in January and February of that year Mortality in this epidemic was particularly high in the elderly and the hospital is situated in an area which was badly affected) But table II shows that the combined mortality rates conceal an important sex difference The over all decline in mortality depends entirely on a fall in female rates (from 38·2% in 1950 to 33·4% in 1953) which offset a smaller rise in the male rates (from 39·5% in 1950 to 42·8% in 1953) The general increase in male mortality depends almost entirely on younger patients however for in the death rates of men aged sixty and over the rise is less definite An unexpected finding was that both sexes had a falling mortality in the seventy five and over age group For this group the death rates per 100 admissions were

TABLE I—MORTALITY IN GERIATRIC WARDS 1950–53

Year	Patients of all ages			Patients aged 60 and over		
	Admissions	Deaths	Death rate	Admissions	Deaths	Death rate
1950	2877	1121	39·0	2256	963	42·6
1951	3216	1301	40·5	2587	1136	43·9
1952	3017	1166	38·6	2522	1034	41·0
1953	2922	1109	37·9	2456	995	40·5

	1950	1951	1952	1953
Men	50·5	48·0	50·3	50·1
Women	48·5	47·0	41·5	39·5

Turnover

The highest annual total of admissions was 3216 in the year 1951—an increase of 339 over 1950 Rather more than half this increase in turnover can reasonably be attributed to the influenza epidemic, for in 1951 there were 173 more discharges as well as 180 more deaths than in 1950 Admissions then declined to 3017 in 1952, and again to 2922 in 1953 Even in 1953 however admissions and discharges remained higher than in 1950, and the downward trend appears to have been checked in 1954 for 1523 patients were admitted in the first six months of that year

The decline in turnover between 1951 and 1953—a difference of 294 admissions—certainly cannot be explained by the small reduction in beds already mentioned; for a loss of 24 beds would account, at 1953 rates of turnover for 138 admissions at most But this type of calculation over simplifies a controversial issue On the one hand some of the improvements obtained in exchange for lost beds might be expected indirectly to increase turnover On the other hand any reduction in beds will tend to reduce admissions and improvements while they may at once increase comfort or convenience, will not increase turnover until this deficit is made good.

TABLE II—COMPARATIVE MORTALITY OF MEN AND WOMEN PATIENTS

Sex	Year	Patients of all ages			Patients aged 60 and over		
		Admissions	Deaths	Death rate	Admissions	Deaths	Death rate
Men	1950	1588	628	39·5	1200	534	44·5
	1951	1716	696	40·6	1316	596	45·3
	1952	1516	617	40·7	1238	538	43·5
	1953	1418	607	42·8	1187	536	45·2
Women	1950	1289	493	38·2	1056	429	40·6
	1951	1500	605	40·3	1271	540	42·5
	1952	1501	549	36·6	1284	496	38·6
	1953	1504	502	33·4	1269	459	36·3

Table III suggests that the decline in admissions during these years depends mainly on falling mortality The decrease in deaths was almost twice as great as that in discharges: moreover if each is expressed as a rate per 100 admissions the death rate fell by 2·6% while the discharge rate increased by 2·3%

These findings illustrate an unpalatable truth—and a growing problem Not every patient whose life is saved in a geriatric unit can be discharged, and falling mortality is likely to reduce the number of patients who can be served by each geriatric bed

The numbers of discharges quoted above include patients transferred to hostels and other hospitals In 1951 337 were transferred but in 1953 only 266 and their corresponding rate per 100 admissions fell from 10·5 to 9·1% In the same period patients discharged to their own homes showed a smaller reduction in actual

TABLE III—TURNOVER

Year	Admissions	Discharges		Deaths	
		Numbers	Rate	Numbers	Rate
1951	3216	[illegible]	59·9	1301	40·5
1952	3017	[illegible]	61·4	1166	38·6
1953	2922	1817	62·2	1109	37·9
Difference 1951–53	−294	−108	+2·3	−192	−2·6

TABLE IV—TRANSFERS AND DISCHARGES

—	1951	1953	Difference
Transferred—			
to other hospitals	81	49	32
to hostels	256	217	39
Total transfers	337 (*10 5%*)	266 (*9 1%*)	71 (*−1 4%*)
Discharged to own homes	1588 (*49 4%*)	1551 (*53 0%*)	37 (*+3 6%*)

numbers and their rate per 100 admissions rose from 49 4 to 53 0% (table IV)

The fall in the transfers to other hospitals presumably reflects the development of Newsham and its growing independence of outside facilities The reason for the fall in transfers to hostels is more complex The number of places in local hostels for the elderly has increased in recent years, yet competition for vacancies seems to increase The turnover in the geriatric wards could probably be slightly higher if there were more hostel vacancies But the main problem arises from patients who, even after all possible active treatment, cannot be discharged to their own homes and are too frail to be transferred to most hostels of existing types It is an encouraging sign for the future that locally, at least, the need for a more sheltered type of hostel is recognised, and the hospital is collaborating with both the Liverpool public-health department and the Liverpool Personal Service Society to augment "half-way" accommodation for "frail ambulants"

Length of Stay

The study of length of stay in geriatric wards is complicated by a few patients who remain for long periods and whose final length of stay was still unknown when this survey was made For example, 56 patients admitted in 1949 or earlier, and a further 23 admitted in 1950, still occupied geriatric beds at the end of 1953 I have therefore divided all admissions into two groups —long term patients who stayed over twelve months, and those who left hospital within this arbitrary limit of twelve months According to this classification, 2 5% of the men, 5 2% of the women, and 3 8% of both sexes admitted in 1950–52 were long-term patients The proportion of each sex increased with age, and in every age group women show a higher proportion than men (table V)

TABLE V—PATIENTS ADMITTED 1950–52 *WITH LENGTH OF* STAY EXCEEDING TWELVE MONTHS

Age	Men	Women	Total
Under 60	15 (*1 4%*)	23 (*3 4%*)	38 (*2 2%*)
60–69	31 (*2 4%*)	36 (*3 8%*)	67 (*3 0%*)
70–79	52 (*2 9%*)	91 (*5 1%*)	143 (*4 0%*)
80 and over	22 (*3 3%*)	74 (*8 4%*)	96 (*6 2%*)
Total all ages	120 (*2 5%*)	224 (*5 2%*)	344 (*3 8%*)
Total 60 and over	*105 (2 8%)*	*201 (5 6%)*	*306 (4 2%)*

Fig 4 shows the *proportion* of long-term patients of different ages in 1950, 1951, and 1952 Though the proportion to total admissions remains about the same, there is a gratifying fall in the numbers and proportion of patients of seventy-five and over staying longer than twelve months

Admitted in 1950	65 patients	(*7 0%*)
" " *1951*	*60* "	(*5 1%*)
" " 1952	50 "	(*4 0%*)

Choosing 1951 as an example, and excluding all long-term patients admitted in that year (4 1% of total), I have shown in fig 5 the mean duration of stay of all other patients—i e , those who left the unit within twelve months In this group, again, there is a remarkably close correlation between age and length of stay Both sexes show a steadily increasing length of stay in cessive age groups, but in every group the average of women was longer than that of men These patie also provide information about the effect on turnover changes in mortality in each sex the average stay before death was much shorter than that before discharge (table VI)

A few of the patients admitted in each year of the survey are still in hospital, *and it is not* yet known to what extent they will influence the average stay of the group As an example of the serious distortion of average values which can be caused by a small minority long stay patients, table VII shows the average stay long term and other patients who left the unit in 19 Of the 3226 patients who died or were discharged, *had an individual stay of less than twelve months* the average stay was 47 days, while 121 long patients had stayed for an average of 970 days, or more than two and a half years A minority of 3 8% long term patients raised the average stay of the 96 2% ma from 47 days to 81 days, and accounted for nearly 45 of the quarter million patient days spent in hospital the whole group

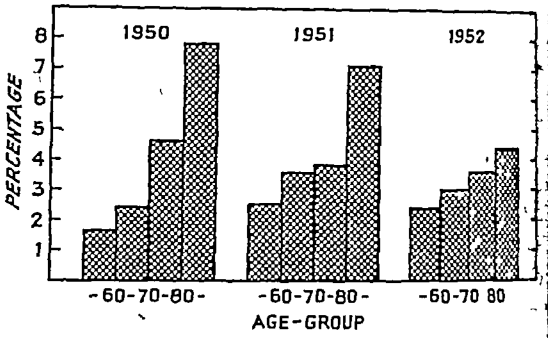


Fig 4—Proportion of each year s admissions with a stay exce twelve months, 1950–52.

Use of Beds

An important group of long term patients fail qualify for inclusion in the usual statistics of admiss discharges, and deaths in any one year In 1950, example, 187 beds were occupied throughout the *by patients who were admitted before* Jan 1 and remained on Dec 31 The number of beds occup throughout a whole year fell to 176 in 1951, but rose

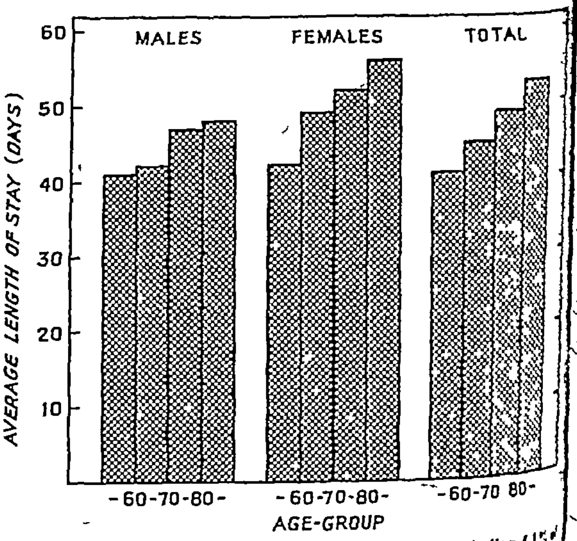


Fig 5—Average stay of patients admitted in 1951, excluding 4 1% total who remained longer than twelve months

TABLE VI—LENGTH OF STAY BEFORE DISCHARGE OR DEATH

—	Average stay (days)					
	All ages			Aged 60 and over		
	Males	Females	Total	Males	Females	Total
Before discharge	52	54	53	56	57	56
„ death	33	46	39	32	46	39
All patients	44	51	47	45	52	48

96 in 1952, and to 201 in 1953 Women patients caused almost the whole of the increase

It is true that most elderly patients occupy beds little longer than younger patients (Graham 1951 Amulree et al. 1952) Almost half (49%) of the patients leaving the unit in 1951 stayed less than one month and 85% had an average stay of less than one month Yet even a small proportion of long-stay patients in the intake of successive years can cause serious cumulative obstruction of beds Although only 3 8% of all patients admitted in 1950–52 stayed longer than twelve months more than 28% of the unit s 707 beds were occupied throughout 1953 by long term patients admitted before Jan 1, 1953 Of the 201 patients who occupied beds throughout 1953, 141 were women (who occupied 35% of 399 beds in female wards) and only 60 were men (who occupied 19% of the unit s 308 male beds) Table VIII shows that 145 (both sexes) had been admitted in the years 1950–52 and 56 in earlier years before the survey began 14 had completed ten years stay by the end of 1953 of whom were under sixty years of age at the time of admission —a reminder that younger victims of chronic disease who need hospital beds for long periods

TABLE VII—AVERAGE LENGTH OF STAY BY A SMALL MINORITY OF LONG-TERM PATIENTS BASED ON PATIENTS LEAVING GERIATRIC WARDS IN 1951

Classification by age and length of stay		Number of patients	% of total	Total patient days	Average stay (days)
All ages	Under one year	3105	96 2	145 640	46 9
	Over one year	121	3 8	117 326	969 6
	Total	3226	100·0	262 966	81 5
Aged 60 and over	Under one year	2474	95 8	118 120	47 8
	Over one year	110	4 2	99 476	904 3
	Total	2584	100 0	217 596	84 2

About a third of all long term patients leaving the unit between Jan 1, 1951 and Dec 31, 1953 were discharged or transferred :

	Discharged	Died	Total
1951	41	80	121
1952	37	73	110
1953	31	68	99
Total 1951–53	109	221	330

These proportions of discharges and deaths give a somewhat gloomy but far from hopeless picture of prognosis in long term patients

The unequal sex-distribution of the long term patients (table VIII) explains most of the apparent difference in the turnover of male and female beds in this series (table IX)

TABLE VIII—LONG-TERM PATIENTS REMAINING ON DEC 31 1953

Year of admission	Males	Females	Total
1952	22	49	71
1951	13	38	51
1950	6	17	23
1949	6	7	13
1948	5	6	11
1947	3	9	12
1946	—	4	4
1945	—	1	1
1944	—	1	1
Before 1944	5	9	14
Total	60	141	201

Demand for Beds

The demand for the unit s beds can be assessed from waiting lists, which have been counted weekly since the beginning of 1951 (table X)

The long waiting lists created by the influenza epidemic in the first quarter of 1951 were virtually cleared by the autumn of that year Thereafter the total numbers waiting in any one season show a steady increase. Once again however, this increase is not evenly distributed between the sexes Men show a slight increase but their rising trend appears to have been checked in the first part of 1954 Women show a greater and more consistent increase from October, 1951 to June 1954 In 1951 male and female waiting lists were about equal, but in 1953 the female list was almost twice as large as the male list

TABLE IX—ADMISSIONS PER BED IN 1953

—	Males	Females	Total
Number of admissions	1418	1504	2922
Number of beds	308	399	707
Admissions per bed	4·60	3 77	4 13
Beds blocked throughout the year	60	141	201
Beds available for admissions	248	258	506
Admissions per available bed	5 71	5 83	5 77

The major deficiency at present is clearly in female beds 90 have been made available in a newly opened hospital, administered by the same management committee and it is planned to increase this accommodation to over 250 beds within the next twelve months.

Discussion

Many social changes contribute to the growing demand for institutional care of the elderly but the basic cause is the changing age distribution of the population The Royal Commission on Population (1949) taking the year 1947 as a datum line and assuming a falling mortality, estimated that people over sixty five years of age would show an increase of 26% by 1963 and of 64% by 1977 The latest statistics show that in 1947–52 these age groups did in fact increase by 7 7%—an annual rate of 1 5%—which is in close agreement with the estimate. Of even greater importance to the hospital services is the redistribution within the age structure of these older age groups Between 1947 and 1952 the number of people aged seventy five and over increased by 14%—almost double the rate of those aged sixty five and over (Annual Abstract of Statistics 1952 and 1953)

TABLE X—AVERAGE WAITING LISTS JANUARY 1951 TO JUNE, 1954 BASED ON WEEKLY COUNTS

Period of year	Males				Females				Total			
	1951	1952	1953	1954	1951	1952	1953	1954	1951	1952	1953	1954
1st quarter	181	66	61	57	133	44	79	111	317	110	140	162
2nd „	21	18	34	34	47	37	65	91	69	49	98	126
3rd „	6	1	21		22	8	29		29	9	53	
4th „	3	10	15		9	36	66		12	44	81	
Whole year	53	24	33		54	27	60		106	63	93	

In the general population as in the present series, increasing age is more obvious among women than among men In these five years women aged sixty five and over increased by 10% men of the same age by only 4% The sex-difference in the age groups over seventy five is less conspicuous but women show a greater rate of increase than males. Although our local population (Merseyside Conurbation) has a lower percentage of elderly people than the national population there are 173 women to every 100 men of over seventy-five on Merseyside, compared with 162 women to every 100 men in England and Wales (Registrar-General 1952)

The high rate of increase in the age-groups over seventy-five affects the hospital services in two ways First, because among the over-seventies there is a sharp increase in frailty, dependence on others, and demand for institutional care (Sheldon 1950, 1954) For example, the 1951 census returns (1% sample) showed that 48% of men remained in whole-time employment after the age of sixty-five, but only 20% after the age of seventy Similarly, the Wolverhampton survey (Sheldon 1948) showed that the proportion of women undertaking the sole domestic care of their household remained fairly constant at about 50% between the ages of sixty and seventy-four, but declined to 40% after seventy five and to 18% after eighty years As long as morbidity continues at present levels, any increase in these older age groups must cause a disproportionate rise in the demand for hospital beds Lowe and McKeown (1950) calculated age specific rates for patients in hospitals for the chronic sick per 1000 of the Birmingham population their rates show a remarkably sharp increase in the older groups

Age	*Rate per 1000*
55–64	1 53
65–74	6 38
75–84	22 21
85 +	58 93

This survey also suggests that an increase in the age of patients admitted to geriatric beds will tend to reduce turnover—both by increasing the proportion of long stay patients and by lengthening the average stay of those discharged

The Wolverhampton survey drew attention to the fact that the lower mortality of old women is accompanied by a morbidity higher than that of old men, and there has since been ample evidence that the proportion of hospital accommodation required for older women is far greater than can be explained by their greater numbers Greenwood (1949), Exton-Smith (1952), Morton (1952), and Andrews and Wilson (1953) all quote examples of the disproportionate demand for female beds, and in the Birmingham survey women had a higher age specific rate than men at all ages after seventy-five

Estimates of future hospital scales based on the total numbers of both sexes, either in the whole population or in the combined age-groups over sixty or sixty-five years, can have only a short-term reliability Long term planning should take account of the changing age-structure and sex distribution of the older population

The difficulties of long term planning have been discussed in a P E P study (1954), which reviews basic assumptions about trends in birth rates and mortality, and suggests that previous estimates of the economic burden of old age may have been exaggerated Fortunately changes in the birth-rate cannot directly increase the burden on the geriatrician for sixty years or more —though the size of the working population will influence the amount of the national income available for welfare services, including hospitals The future demand on the hospital services will depend both on the numbers of old people alive, and on the incidence of disease among them It is a melancholy thought that many of the problems of old age are a by-product of unbalanced medical progress We can prevent or cure many of the diseases which used to kill we cannot yet control many of the more insidious diseases which disable those who survive into an extended old age The control of arterial degeneration would probably do more than any other scientific advance to reduce the social and economic problems as well as the suffering of old age Extra longevity without lower morbidity is a doubtful blessing for most of us Old age must be made healthier and more useful if it is to be anything but an increasing burden, both to the individual and to the community

It is a pleasure to acknowledge the willing assistance of many members of the hospital staff I am especially indebted to Miss C Ledsham and others who helped in the tedious work of extracting the basic figures for this survey

REFERENCES

Amulree, Lord Arnold, P, Polak A (1952) *Lancet*, ii, 191
Andrews, C T, Wilson, T S (1953) *Ibid* i 785
Annual Abstract of Statistics (1952 and 1953) H.M Stationery Office
Exton-Smith, A N (1952) *Brit med J* ii, 182
Graham, W L (1951) *Lancet*, ii, 931
Greenwood, J M. (1949) *Ibid* ii 1047
Lowe C R, McKeown, T (1950) *Brit J soc Med* 4, 61
Morton W (1952) *Brit med J* ii, 715
Political and Economic Planning (1954) No 364, see *Lancet* 1954, ii, 278
Registrar General (1952) *Statistical Review of England and Wales* H M. Stationery Office
Royal Commission on Population (1949) Report H M Stationery Office
Sheldon, J H (1948) The Social Medicine of Old Age London.
— (1950) *Brit. med J* i, 319
— (1954) *Lancet* ii, 151
Thomson, A. P (1949) *Brit med J* ii, 243

SALARIES IN THE PUBLIC-HEALTH SERVICE

UNDER an Industrial Court award which operates as from Jan 1, 1955, medical officers of health, senior medical officers, and medical officers in departments (assistant medical officers) are to receive increases in salary ranging from £175 to £200 The new salary scales are as follows

Medical officers of health

Population Group	*Commencing salary*	*Increments*
Not exceeding		
75,000	£1625–£1830	4 × £51 10s
100,000	£1730–£2040	6 × £51 10s
150 000	£1940–£2250	6 × £51 10s
250 000	£2150–£2450	2 × £100 1 × £50
400,000	£2400–£2700	2 × £100 1 × £50
600,000	£2500–£2900	3 × £100
Over 600 000	At discretion	At discretion

Senior medical officers
£1415 × 50–£1765 × 65–£1830

Medical officers in departments (assistant medical officers)
£975 × 50–£1375

The court found against a proposal to introduce in Scotland a salary scale for a medical officer of health with a population group not exceeding 60,000

WHOLE-TIME AND PART-TIME CONSULTANTS

THE Joint Consultants Committees have had recent discussions with the Ministry of Health and the Department of Health for Scotland about whole time and maximum part time service for consultants in the National Health Service, and the following is an agreed statement of the position

It is recognised that some consultants, while prepared to devote substantially the whole of their time to hospital work and to give it priority on all occasions, would prefer a maximum part-time to a whole time contract Ever since 1948 it has been the Ministry's view that, subject always to the needs of the hospital service, employing boards should in this matter take into account the circumstances and preferences of the consultants concerned While there has been no previous statement on this point as regards Scotland, the practice in that country has been similar

Where a new appointment is being made this means that, except where the board decides that the needs of the hospital service (considered in conjunction with the needs of the local health services where the consultant is to undertake duties on behalf of a local authority) demand a whole time appointment, the competition should be thrown open to all applicants who are prepared to give substantially the whole of their time to the post, whether they prefer a whole-time or a maximum part-time contract In such a case the successful candidate should e asked to state his preference until after he has been elected for appointment

Similarly, if a consultant who is already employed in whole time post wishes to transfer to a maximum part-me contract, or vice versa the board should, before eaching a decision, take his circumstances and preferences ito account again subject to the overriding needs of he hospital service.

This statement does not, of course deal with the many ses where the services of a consultant are needed in the ggregate for only a limited volume of work and where erefore a part time appointment would in all cases be ppropriate.

Public Health

Vaccination in London

At a meeting of the London County Council on April 20 was stated that the percentage (based on live births) of London children under 1 year vaccinated against smallpox hows a steady improvement since 1949 The figures re as follows:

1949	25%	1951	38%	1953	48%
1950	32%	1952	45%	1954	49%

There is continual propaganda on the part of the ouncil's health visitors and clinic doctors to persuade others to have their young children vaccinated General ractitioners are encouraged to take their part in vaccina on and are paid a fee of 5s for each notification sent to e council. Opportunity is also taken to encourage accination by the distribution of literature and display appropriate material in council establishments

Notification of Tuberculosis

A recent Ministry of Health memorandum [1] explains hich medical officer of health should be notified when a erson is diagnosed in hospital as suffering from tubercu sis. Notifications should usually be sent to the medical ficer of health of the district in which the patient ormally lives; but where in the case of long-stay atients, the hospital itself can reasonably be regarded the patient's place of residence the notification should e sent to the medical officer of health of the district in hich the hospital is situated.

Swedish Poliomyelitis Vaccine

s we reported a fortnight ago [2] plans are going ahead Sweden for the use of a poliomyelitis vaccine made growing virus on human tissue Further details have en given in a report by Prof Gunnar Olin of the edish State Bacteriological Laboratory The virus as been grown on aborted human fœtal tissue, and then activated with formalin (1 in 2000 compared with the in 4000 formalin recommended by Salk) The inacti ation is performed at 25 C (the American workers refer 37°C) The antibody response is said to be good hough vaccine has been prepared to immunise 120 000 hildren, but further supplies may be limited by the hortage of suitable tissue for culture American vaccine ay be imported for the time being

Education of Physically Handicapped

The Ministry of Education[3] has found that on Oct 1 951 1052 children were awaiting places in special schools. Their disabilities were as follows: cerebral palsy 485 oliomyelitis 100 heart defects, 78 muscular dys-rophy 73; spina bifida, 68 hydrocephalus, 42 eformities, 40; hæmophilia 20 fragilitas ossium, 20 uberculosis 10; Perthes's disease 12 muscular atrophy, ; rheumatoid arthritis, 3; others 83

Of the 1052 children 202 were awaiting places in day chools and 850 in boarding schools. The existing ducational arrangements for these children were as ollows: 371 were receiving home tuition 250 were n ordinary schools; and 106 were receiving some other ype of special educational treatment (mainly in hos pitals). Of the 725 unprovided for some were not receiving home tuition because of difficulty in finding teachers or of unsuitable home conditions

There appeared to be enough places in day special schools There is still a shortage of places in boarding schools but additional places expected to come into use within the next two or three years should suffice for all children whose parents are likely to consent to their attending such schools

First Quarter in England and Wales

The Registrar General, in his provisional figures [1] for England and Wales in the first quarter of 1955, records a birth rate of 15 5 per 1000 population, compared with 15 9 per 1000 in the first quarter of 1954 The death rate was 15 4 per 1000 population, as against 14·0 per 1000 in the first quarter of 1954 The infant-mortality rate was a new low record for a March quarter—29·0 per 1000 related live births It was 31·0 per 1000 (the previous record) in the first quarter of 1954 The stillbirth rate was 23 1 per 1000 live and still births compared with 23 7 in the corresponding quarter of 1954

Parliament

Disseminated Sclerosis and War Pensions

In the House of Commons on April 20 Mr Arthur Moyle asked the Minister of Pensions and National Insurance to examine the rules and the present terms of the Royal Warrant to see whether ex-Servicemen with disseminated sclerosis might not be assessed at the 100% disability rate—Brigadier J G Smyth joint parliamentary secretary to the Ministry pointed out that in the first world war two-thirds of the casualties were wounds In the second world war the causes of two thirds of the pensionable cases were diseases. But to earn a war pension these diseases must be causally connected with service There was no evidence that disseminated sclerosis was in any way a military disease. The Ministry tried, however, to stretch the regulations as far as they could and where a man had been subjected to a sudden shock, and within a short period showed signs of disseminated sclerosis they said that perhaps the shock, although they knew it had nothing to do with the disease had accelerated its progress and pensions were granted for aggravation Accordingly after the late war pensions for aggravation of disseminated sclerosis were awarded in 1538 cases and there had been 1117 rejections.

QUESTION TIME

Ban on Heroin Imports

In the House of Lords, replying to a question Lord Mancroft said that except for small quantities for purely scientific purposes Her Majesty's Government had decided not to permit the manufacture and export of heroin after Dec 31, 1955 As adequate supplies had hitherto been manufactured in this country imports of heroin had not been authorised for many years: it was intended to maintain the prohibition on importation. The Government had taken this decision in order to give effect to a resolution adopted by the Economic and Social Council of the United Nations at its 18th session, urging all governments to prohibit the manufacture export, and import of this drug except for scientific purposes. Before the decision was reached the advice of the appropriate statutory advisory bodies was taken.

Viscount Elibank Are the Government aware that Dr Arthur Douthwaite senior physician at Guy's Hospital, has stated in the *British Medical Journal* that the banning of this pain killing drug heroin, is an astonishing move which will inflict much hardship upon a multitude of patients? Is the noble Lord aware that one of the best known physicians in Edinburgh, Dr A B Flett has written to me saying it is iniquitous that this most useful, and often, in certain cases really necessary drug should be banned?—Lord Mancroft: The Government are aware of these opinions On the other hand I understand that adequate supplies of perfectly good substitutes for this drug are now available The purpose of the action is, of course to facilitate the world wide banning of traffic in this extremely dangerous drug

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[1] HM(55)33.

[2] Lancet, April 23 1955 p 857

[3] Ministry of Education: administrative memorandum no. 503 April 25 1955

[1] Registrar-General weekly return no 15 1955 H.M Stationery Office 1 p. 20 1s

I do not think that the Government can do more than follow the technical advice and guidance given by the Central Health Services Council, the Standing Medical Advisory Committee, and the appropriate bodies in Scotland and Northern Ireland

Poliomyelitis Vaccine

Replying to questions, Mr **Iain Macleod**, the Minister of Health, said that a small field trial with the Salk poliomyelitis vaccine was being carried out by the Medical Research Council All vaccine used in this trial, whether imported or manufactured here, would first have been the subject of rigorous tests by the council Plans for large scale immunisation were, of course, dependent on the Minister of Health being satisfied, so far as was humanly possible, as a result of these tests and trials that the vaccine to be used was both efficient and free from danger

Mr **Eric Fletcher** Would the Minister say whether any supplies of Salk vaccine from the Cutter Laboratories have been received in this country?—Mr **Macleod** No Cutter vaccine has been received in this country

Mr **Mont Follick** Are the vaccines which are being made by the Glaxo Laboratories of their own special prescription, or according to a prescription imported from America?—Mr **Macleod** I understand that what they are making is, in fact, the Salk vaccine The difficulties in this case have arisen, I understand, from a batch made by the Cutter Laboratories As we have none from those batches in this country, there should not be difficulty in that particular direction

Salaries of Hospital Pharmacists

Replying to questions Mr **Macleod** said that a general agreement on increased salaries for hospital pharmacists was reached by the appropriate Whitley Council on April 20 Details were now being worked out

General Practitioners in the N H S

Replying to questions, Miss **Patricia Hornsby Smith**, parliamentary secretary to the Ministry of Health, said that on July 1, 1954, 19,300 general practitioners were practising in the National Health Service Altogether 837 doctors practised single handed and 614 partnerships employed assistants, other than trainees The Minister of Health was not prepared to limit the increased number on a list when an assistant was employed to a maximum of 1500 The relationship of principals and their assistants could not readily be regulated by statute

Mr **Somerville Hastings** Does not the Minister realise that many doctors find great difficulty in getting the necessary capital to start in practice and are therefore liable to be exploited by doctors who employ them as assistants?—Miss **Hornsby Smith** The matter is being considered by the British Medical Association and the Medical Practitioners' Union, but we have had no decisions or opinions from them yet

Mr **H Marquand** Does the hon lady recollect that it was a definite promise by the medical profession at the time when the payment to general practitioners was referred to adjudication that they would seek to reduce the number of assistants and increase the number of principals in practice? Is she satisfied that the medical profession are giving real coöperation in this matter as they undertook to do?—Miss **Hornsby Smith** There has been an increase in partnerships and a reduction in the number who do a long period as assistants These consultations are going on between the B.M.A and the M P U and I think the profession are coöperating in this matter where they feel that there is hardship Mr **Hastings** said that the B M.A. committee had already reported and their report was by no means entirely happy about the situation

Replying to a further question, Miss **Hornsby Smith** said that on July 1, 1954, 131 assistants were still in posts which they had taken up before July 1, 1949 Mr **Hastings** Does not the Minister think that this is a serious matter? Even her own figures show that While it is admitted that doctors may derive a good deal of benefit from being assistants for a time, does she not agree that for them to go on year after year in that position, as these figures suggest, is a very dangerous situation?—Miss **Hornsby Smith** I think we should keep this matter in proportion There is a steady increase in the trend towards partnerships Mr **Marquand** Would it not be possible to make an inquiry into this comparatively small number of cases to see what the reason is for this long period of assistantship?—Miss **Hornsby Smith** We will consider that point

Lung-cancer Mortality

Replying to a question, Mr **Macleod** said that the provisional number of deaths attributed to cancer of the 1954 was 16,332 The numbers of deaths so attributed in and 1944 were 2775 and 6684

Mr **Hastings** Does the Minister realise the importance to the health of the community resulting from his pronouncements on this subject some few years ago? Will he consider making a similar pronouncement setting forth the increased knowledge up-to date resulting from research?—Mr **Macleod** I recognise the public anxiety here and I shall be very glad to consider the suggestion

Dr **Barnett Stross** Would it not be true to say that whatever may be the cause of this disease—and many people now suspect what may be the cause—it cannot be the ingestion of any foodstuffs that is causing the rise in cancer of the lung for it would affect women as well as men, and that it does not do?—Mr **Macleod** Whatever may be the reason, it is true that the increase is very much more—indeed it is more than twice as great—amongst men than women, which would seem to indicate a special cause

Child's Treatment in Hospital

Mr **Kenneth Robinson** asked the Minister why a boy aged 10, who was admitted to Hampstead General Hospital on March 30 with a fractured and dislocated arm, received no medical attention for more than six hours, during which time he was offered neither food nor a sedative—Mr **Macleod** replied I am very much afraid that the facts are as stated and it is clear that the hospital staff failed grossly in providing proper attention On behalf of the board of governors and myself I must apologise to the child's parents I assure them that the board take a serious view of the whole incident and that those responsible have been severely reprimanded

Mr **Robinson** Whilst I welcome the Minister's admission of the responsibility of the board of governors for this matter, and, of course, accept his assurance of regret does he not agree that the public has been led to expect that the teaching hospitals should set a standard of conduct in these matters, and does that not make the incident even more deplorable?—Mr **Macleod** No doubt that is true I am bound to say that the only thing I welcome about this case is that the hospital at once admitted an error As we know errors happen in the hospital service I deeply regret that this should have happened, and my views have been put very strongly to those concerned Mr **Hastings** Will the Minister make it quite clear that it is his desire that at every general hospital there should be a medical cover throughout the twenty four hours, and that so many doctors should not be away from their work as at present?—Mr **Macleod** It is certainly desirable that wherever possible cover should be provided, if not on a twenty four hour basis, at least urgent and near

Requests for Lists of Patients

Replying to a question, Miss **Hornsby Smith** said that the Minister of Health was not aware that political party organisations were asking doctors for lists of patients for the purpose of the postal vote at the general election

Mrs **Barbara Castle** I have in my possession circular letters from Conservative associations to local doctors in their areas asking them to supply the Conservative party with the names of blind, sick, and aged patients on their registers in order that they may be contacted with a view to their having a postal vote Will the Minister institute an immediate inquiry and inform the doctors that this is contrary to professional etiquette and their duty to their patients?—Miss **Hornsby Smith** If the hon lady will let the Minister have the evidence I can assure her that he will look into the matter The vote is secret and in their individual capacity it is certainly helpful to see that as many as possible obtain their vote

Mr **Herbert Morrison** Will the hon lady on behalf of the Minister give an assurance that neither directly nor indirectly will those associated with the National Health Service be coöperators with any political party organisation in connection with the forthcoming election? Is she aware that there was the strongest impression at the last election that such malpractices took place?—Miss **Hornsby-Smith** I can certainly give the assurance that the Health Service will not be used in this way

Replying to further questions, Mr MACLEOD said he would look into this matter at once Whether he would make a statement on it would depend on the results of his inquiries.

Orthodontic Treatment

Replying to questions Miss HORNSBY-SMITH said that the number of courses of orthodontic treatment approved under the National Health Service for 1040 was 12 000 and the payments made were £300 000 The figures for 1954 were 48 000 and £500 000 Orthodontic treatment was provided under the hospital and specialist services, the school health service and the general dental services. The number of dentists in England and Wales who in 1954 were each given approval to start more than 100 courses of orthodontics under the general dental services was 42

Medical Examination of Broadmoor Prisoners

Mr T E DRIBERG asked the Home Secretary if he was aware that a medical report by the principal medical officer of Brixton Prison dated Feb 14 1953 stated that a prisoner was sane and fit to stand trial on a charge of attempting to murder his wife and recommended him as suitable for voluntary treatment in a mental hospital; that at his trial five days later this man was found guilty but insane and ordered to be detained during Her Majesty's pleasure and that he is still detained at Broadmoor where his wife and other relatives had found him in apparently normal health and if in these circumstances, he would allow an independent medical examination of this patient.—Major LLOYD GEORGE replied The responsibility for deciding when a Broadmoor patient is fit to be transferred or discharged rests on the Home Secretary and my predecessors and I have consistently taken the view that the expert staff of psychiatrists at Broadmoor who have the patient under constant observation are in a better position than an outside doctor to advise the Home Secretary on the patient s mental state and future prospects. The answer to the last part of the question is, therefore No Sir

Mr DRIBERG Is the Home Secretary aware that Dr Mathieson, of Brixton, also said that this man was suffering simply from a mild anxiety neurosis, which should yield to proper psychiatric treatment but that since he has been in Broadmoor he has had no such treatment whatever? It is obviously impossible for the very efficient and conscientious staff at Broadmoor to give proper psychiatric treatment to the very large number of patients with whom they have to deal In the circumstances, will the Home Secretary consider either getting an independent opinion or transferring the man to a mental hospital where he can be treated?—Major LLOYD GEORGE: These cases are very difficult I am aware of the opinion to which the hon Member has referred and I have of course gone into the case myself with great care On the information I have I do not think anything can be done But I am prepared to look at the matter again and I will do so

Motoring Offences and Blood Tests

Replying to a question, Sir HUGH LUCAS TOOTH, joint under secretary of State to the Home Office said that during the last year no motorist charged by the Metropolitan Police with being under the influence of drink while in charge of a car had requested a blood test but in one case samples of blood and urine were taken at the request of a doctor called on behalf of a person who had been arrested for such an offence

Mr SOMERVILLE HASTINGS: Does the Minister not agree that this test which has been largely used in other countries, might usefully be *tried* out in this country so that some idea could be obtained of its real value? At present its value seems to be somewhat uncertain. Will the test be made possible for those who apply for it?

Sir HUGH LUCAS TOOTH: Opinion about the value of blood tests in these cases is sharply divided, and it would be inappropriate for me to express a view either way at the present time Research on the effects of alcohol upon driving performance is being carried out by the Medical Research Council and the Road Research Laboratory

Mr R. R. STOKES: Have not the police chucked this bit of nonsense as being absolutely unreliable?

Replying to a further question Sir HUGH LUCAS TOOTH said that the provisional figures showed that in magistrates courts in England and Wales there were during the first nine months of 1954 1051 convictions of driving or being in charge of a motor vehicle while under the influence of drink or drug The number of resulting sentences of imprisonment was 112

In England Now

A Running Commentary by Peripatetic Correspondents

THEY say a psychiatrist is a man who goes to the Folies Bergère to look at the audience, so I went to the Private View day at the Royal Academy The trouble about Private View day is that you get trampled underfoot by people with one eye on the pictures and the other on the look-out for their friends But still, it has the advantage that the ladies hats are more surprising than they are on other days, and the girls seem prettier and you can watch the artists being casual about their masterpieces They have a variety of techniques for this. I heard one ask, in incredulous tones, ‘ Do you mean you *like* it? but whether this was modesty, or surprise that his audience appreciated it, I could not tell. Then I like to see the subjects standing sheepishly near portraits of themselves. I am one of those people who do not get much further in Art than knowing what they like, but I did like the portraits this year there were several startlingly good ones and very few of those others. I liked the one of the toy monkey because he unlike most of the other sitters, was not pretending to be blase about having his picture painted There were, of course, the usual dreary people sitting in dreary rooms, but I wonder how Charles Spencelayh manages to make ordinary objects so exciting? I suspect that the secret lies in the title he has given to one of his groups—*God's Good Things* Perhaps it is because I like bouncy dogs, but I was intrigued by *Whippet* in terra cotta, who had curly ears and a curly tail and was very much alive ‘ And ducks are soothy things, and lovely on the lake That was another lovely thing in oak, a mother duck obviously telling her brood a bedtime story Exciting in a different way is a statue of a nun, with severe straight lines except for her face and expressive hands. There is so much too much, to take in as always The biggest crowd was consistently round what has now come to be known as the Annigoni of the Queen For the record the most frequent remark I heard in the whole exhibition was The traffic my dear, was simply frightful.

* * *

My medical wife and I discussed the mushrooms fully Growing they were pleasant-looking things and after consulting the encyclopædia we convinced ourselves that they were edible We ate them for breakfast the following day and I had a large helping which tasted delicious with bacon My wife drove me to the hospital where I sat down in the office to attend to some routine papers Some thirty minutes after breakfast the odd feeling started I found it difficult to concentrate on my work and noticed a transient diplopia which could be mastered only by an effort. I experienced a curious sensation of being in the room but apart from my body The voice of someone speaking in an adjoining office seemed a great distance away Of course this disturbed me but the probable cause eluded me for a while. Then—The Mushrooms! I grabbed the phone and with some difficulty dialled my home. With great relief I heard my wife s voice, though it was slurred and not too intelligible. In the brief moments of waiting for her to answer I had an awful vision of her having crashed the car on the way home. She too felt very odd and had just realised why By this time I was getting a bit disorientated but I sent one of my colleagues off to bring my wife my daughter, and the lodger into hospital I then floated rather than walked up to the ward for a stomach pump session. I was given atropine and intravenous glucose and rapidly felt better

My wife who was not treated so soon became quite confused and went into a state of shock before she reached hospital but fortunately retained enough presence of mind to insist on picking up the lodger from her office on the way The three of them were then treated as I was, to the intense indignation of daughter aged eight who had eaten only one small mushroom and felt quite well They too improved rapidly, but my wife remained mildly shocked for several hours

I found it impossible to get the fungus identified but assumed that it was one of the types containing a mus carine-like alkaloid—possibly *Inocybe patouillardi* I don't think it could have been *Amanita muscaria*, which from its pictures seems a distinctive fungus quite unlike our specimens

The story spread rapidly and, needless to say, such an occurrence in a medical family was the cause of much ribald comment The loudest laugh was enjoyed by my son aged twelve who doesn't like mushrooms and who refused them on this occasion because he didn't like the look of them His big moment came when he poked his head into my hospital room and said "I told you so!"

* * *

Some of our West End colleagues still bemoan the loss due to war, the B B C , and Big Business, of the Langham, and now the Bolivar—its posteriorly situated vestigial remnant—has suddenly closed its hospitable doors It is heart-rending to see thirsty pillars of our profession being caught out by padlocked doors without so much as a "closed" notice on them I saw one famous man nip round the corner to check his watch against the All Souls' clock before the devastating truth dawned upon him Where consultants' fluid-balance and milli-equivalents can conveniently be put in order now, goodness only knows What with this calamity and the Med Soc Lond having no visible means of support at its northern end, Chandos Street is not what it was

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Those who heard Pierre Monteux conducting the Royal Philharmonic Orchestra at the age of 80 must have marvelled at his apparently limitless energy Bruno Walter, one year younger, is to take command of the B.B C Orchestra this month It is only a few years since Toscanini, now 88, electrified us all at the Festival Hall Vaughan Williams, at 83, would probably call himself an amateur conductor only Weingartner, Mengelberg, Richard Strauss, and Kussevitzky were all around, or well above, 80 when they died in full harness Sir Thomas, of course, is a mere stripling at 75 , he, Cameron, and Ansermet are a trio of active septuagenarians Sir Henry Wood had hardly shed any of his habitual load of work when he died at 75

It is fortunate for the rest of us that these eminent maestros enjoy such long spans But why do they? Is it because, unlike most surgeons and professors, they keep on working? Or are eminence and longevity associated irrespective of occupation? Quite apart from ex-prime ministers, Augustus John and Brangwyn are well into their eighties , Sir Gerald Kelly and Sir Alfred Munnings are in their late seventies

A famous but still relatively young conductor once told me that, while in action, he felt "the vital juices flowing down the arms to the heart" Perhaps he was right , perhaps the apparent immunity of orchestral conductors to the more spectacular forms of cardiovascular collapse is due to the fact that they wave their arms about a good deal

* * *

How much we suffer from failure to convey our wishes correctly to our patients Listening to one's colleagues shows how much time and effort are wasted by lack of liaison -

"Lie on your back on the couch—No, on your back, please"

"Show me where the pain comes—No, on your own back please"

"Please stand up—now, raise your right leg—thank you, and now your left leg—thank you, and now get up off the floor"

There is clearly an urgent need to revise the technique of medical questioning, and at the next twelve unselected outpatient clinics we are giving a trial to the following phrases

"Lie on the couch with your tummy upwards"
"Show me on your own back where the pain is"
"Bend your knee crooked—and now bend it straight"

I would welcome suggestions how to avoid the inevitable contraction of the calf muscle just as I withdraw the tendon hammer from my pocket "Relax," "Pretend you're asleep," "Don't bother about me," "Go loose," and "Pretend you're dead" have been tried and found wanting

Letters to the Editor

HASHIMOTO'S STRUMA LYMPHOMATOSA

SIR,—Independently, we have each been interested several years in Hashimoto's "struma lyphomatosa" 1953, again independently, we obtained marke abnormal liver-function tests in some of these cases, finding of which we have seen no previous record, and which one of us drew attention in your columns year[1] This mutual interest came to light when we by chance on the slopes of a Yorkshire mountain, not having met as colleagues for over twenty years intend to record our findings in full in due course but preliminary details may interest your readers

Owing to a difference of approach there is some of uniformity in our case records, but we are agreed the main observations

(1) The presumptive diagnosis is essentially clinical the condition is commoner than is generally suppos Although there are certain typical features, includ preponderance of cases in middle aged females, sympto of subthyroidism of variable degree, and a thyroid easily felt and abnormally firm, we would stress that infrequently the patient first visits her doctor for symp toms not quickly ascribed to thyroid disturbance, as lassitude, muscle and joint pains, increasing weig and changed facial appearance The efficacy of mode treatment by oral dried thyroid emphasises the need the diagnosis of Hashimoto's disease to be consider more readily We have studied about 25 patients, nearly two thirds of whom the diagnosis has confirmed by surgical section

(2) The basal metabolic rate is subnormal in most the patients when first seen, but a minority in the stage show signs and symptoms of hyperthyroidis Anæmia is not a characteristic feature

(3) The liver function test most consistently abnorm in the untreated patient is the colloidal gold te thymol turbidity and flocculation tests generally parallel with it In a few patients the serum alka phosphatase is slightly or moderately raised Th bromsulphalein test may be abnormal, but the galact tolerance has been normal in the 5 patients exami After treatment by dried thyroid gland, the liver-func tests in some patients return to, or towards, nor within a period of months, but in others the return much slower and we have seen the tests still gro abnormal after more than two years Electrophor shows a raised and abnormal serum-globulin level in few patients In general, however, there appears to no close relationship between the results of the flocc tion test and the plasma cholesterol, or the bas metabolic rate

(4) We suspect that gross liver disease may arise struma lymphomatosa One of our patients, observed seven years, now has a liver which is greatly enlarg and abnormally firm, and a palpable spleen The sple is palpable in 2 of 17 other patients In the 1 patient whom surgical biopsy of the liver has been poss however, the histology was normal

(5) We have not yet seen such gross changes in th liver-function tests in typical primary myxœdem although lesser degrees of change have been observed.

(6) We are impressed by the steady diminution the size of the thyroid gland during treatment by dr thyroid , this point is not mentioned in the literatu but it was emphasised by Crile in his Moynihan lectu to the Royal College of Surgeons in January, 1954

Department of Pathology,
General Hospital,
West Hartlepool
R T COOKE

Crumpsall Hospital,
Manchester
R W LUXTO

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[1] Cooke, R. T , Wilder E *Lancet*, 1954, i 984

STAPHYLOCOCCAL INFECTION IN THE NEWBORN

ir,—We fear that others, like ourselves may interpret paper by Dr Forfar and his colleagues (March 19) simply as a clinical and bacteriological study but as a ommendation that all infections in newborn babies in ternity hospitals should be treated with erythromycin feel that such a recommendation would be misguided we should like to comment upon it The clinicians ongst us made the mistake of adopting just such a icy some years ago and we have lived to see its fortunate long term consequences We have also rnt more about the nature and dangers of staphylococal infection in the newborn as a result both of close llaboration between clinicians and bacteriologists and more critical clinical observations in our hospital during past few years We accordingly reversed our previous icy some time ago, and have as yet had no cause to ret this decision The fact that the antibiotic with ich we were concerned was penicillin not erythrocin does not appear to be relevant since as Forfar d his colleagues admit, there is evidence that sooner later staphylococci become resistant to erythromycin

For us the crucial fact is that the more frequently the phylococci in a particular community are exposed to a ticular antibiotic, the more likely are they to become istant to that antibiotic. If there were any overriding vantages to be gained by using an antibiotic as freely Forfar and his colleagues recommend the inevitable advantage would have to be accepted But although y state that "Edmunds et al (1955) show that early gnition and early treatment of minor staphylococcal ction in the newborn play an important part in venting serious sepsis" we can find no evidence atever to support this statement in the paper to which y refer[1]

We have not treated any case of skin sepsis when t seen during the past twenty months unless it was extensive pustular rash in a small premature baby, we had other grounds for believing that the baby ill

uring this period 163 cases of skin sepsis have occurred tules and paronychiæ): 11 were treated from the start use of one of the indications we have mentioned 11 e treated later because the local lesions were extending r a period of forty-eight hours observation and the aining 141 cases (86%) received no treatment of any kind n they remained well and the local lesions were clearing or cleared after forty-eight hours.

During the same period of twenty months virtually all s of sticky eye developing after the first twenty four rs of life were treated simply by local instillation of 10% phacetamide The cases which developed within the first nty four hours were left untreated unless they failed to lve spontaneously during a period of forty-eight hours ervation because we know as a result of earlier work in this spital[2] that a *Staphylococcus aureus* can be cultured from than 10% of these early cases. Altogether 470 cases of ky eye were recorded during the twenty months.

We should like to mention that no serious infection of y kind (pneumonia, osteitis &c) developed in any of e 633 babies suffering from a superficial infection and ated on the conservative lines we have indicated

We did encounter a serious infection during this riod in a baby who died of a staphylococcal pneumonia the thirteenth day of life but there was no clinical perficial infection in this baby at any stage We also d to use a systemic antibiotic on a number of occasions cause a baby appeared to be ill and probably infected the absence of any minor superficial infection whatever We feel that this experience supports our present licy of restricting the use of all antibiotics to an absolute minimum since it has shown that this is not only desirable in theory but also safe in practice The real indication for antibiotic therapy seems to us to be a clinical diagnosis of systemic infection (with or without superficial sepsis) This indication is uncommon, but an effective antibiotic must be used at once in these circumstances and this is an urgent matter on which the baby's life may depend We feel that our chance of being able to use any particular antibiotic with confidence (before the sensitivity of the organism from the particular case is known) depends upon our past conduct in relation to that antibiotic. We are very glad to be in a position to keep erythromycin in reserve for the case that really needs it and whose life may very well depend upon it and we would like to think that others were exercising a similar restraint We cannot understand what has prompted Forfar and his colleagues to reverse the much more selective policy which they outlined in 1953[3]

S D M Court
C A Green
J G P Hutchison
G A Neligan

Princess Mary Maternity Hospital
Newcastle upon Tyne

ACID-FAST BACILLI IN ACHALASIA OF THE CARDIA

Sir,—Dr Davies and Dr Roberts (April 23) rightly emphasise the need for critical assessment of the finding of acid fast bacilli in the sputum in cases of achalasia of the cardia with respiratory symptoms A diagnosis of pulmonary tuberculosis may wrongly be made if such organisms are not cultured

Acid fast saprophytes are not uncommon findings in sputa in a number of other chronic pulmonary diseases and it is doubtful if they play any important rôle in them. In the lipoid aspiration pneumonia of achalasia of the cardia however, these organisms may act as pathogens and the bacteriological findings must not be summarily dismissed A fatal infection of this nature and a review of the subject has been published[4] Although mycobacterial strains freshly isolated from such cases generally show an unusual virulence for experimental animals especially mice it is the modification of the host's response brought about by the presence of fat in the pulmonary alveoli coating the organisms that appears chiefly responsible for the resulting illness. The cultural characters of the strains isolated vary from case to case and so these pulmonary infections differ from some of the recently reported non tuberculous mycobacterial skin infections such as that due to *Mycobacterium balnei*[5]

Institute of Pathology
Queen's University of Belfast

James B Gibson

A BARBITURATE ANTAGONIST

Sir —I have read with interest the letter of Dr Morgan McElligott (April 16) in which he reports no change other than a deepening of respirations after the administration of 240 mg of ββ methyl-ethyl glutarimide ('Megimide') to a patient who had taken gr 72 of phenobarbitone Dr McElligott is not quite correct in thinking that the lack of clinical improvement was due only to insufficient dosage Certainly the dose for this case would have been 1 0 g and probably even then the patient would have regressed and required one or two treatments more But the important point is that treatment was not started until *six* days after admission

Megimide appears to be a specific antagonist to barbiturates. At the end of six days there would be little barbiturate in the body By this time however, there would have been extensive cellular damage—e g, cerebral œdema—and one would not expect any drug to reverse this injury

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Edmunds P N Elias-Jones T F, Forfar J O, Balf C L *Brit med J* April 23 1955 p 901

Hutchison, J G P Bowman W D Unpublished data

[3] Forfar J O Balf, C L Elias-Jones T F Edmunds P N *Brit med J* 1953 ii 170

[4] Gibson, J B *J Path. Bact* 1953 65 239

[5] Linell F Norden, A *Acta tuberc scand* 1954 suppl no 33

Since we commenced using megimide we have treated fifty cases Two are noteworthy In the first the patient had taken gr 100 of phenobarbitone and treatment was not started until thirty-six hours later This was a difficult case, and ten treatments were given before the patient recovered In the second case gr 114 of quinalbarbitone was consumed, but the patient was treated within three hours An uneventful recovery ensued with one treatment

Department of Pharmacology,
University of Melbourne, Australia
F H SHAW

A VISIT TO KOLTUSHI

SIR,—Mr Ruscoe Clarke and Dr Leonard Crome (April 2) write that the objective of study at Koltushi "*was an understanding of the functioning of the organism in its unity with the environment*" They state that among the "general principles" used at Koltushi one was expressed in the statement "Descartes knew already that environmental factors determine the functioning of the organism by means of reflexes" In their conclusion, they state that they "had no more than a glimpse of the new science" They ask "was it a glimpse into the future?"

We are entitled to ask whether a science based on the study of the "conditioned reflex" is so new Is it a study likely to provide the kind of future we should all desire should come about? In his introduction to *The Use of the Self* by F Matthias Alexander, the late John Dewey wrote in 1932

> "The school of Pavloff has made current the idea of the conditioned reflex Mr Alexander's work extends and corrects the idea It proves that there are certain basic, central organic habits and attitudes which condition every act we perform, every use we make of ourselves This *discovery corrects the ordinary conception of the conditioned* reflex The latter as usually understood renders an individual *a passive puppet to be played upon by external manipulations* The discovery of a central control which conditions all other reactions brings the conditioning factor under conscious direction and enables the individual through his own coördinated activities to take possession of his own potentialities It converts the fact of conditioned reflexes from a principle of external enslavement into a means of vital freedom."

Mr Alexander enables a person to provide for his use a self acting as a unity with its environment by the following procedure

> The person inhibits his habitual *reaction* to a stimulus Thus he allows the head to go forward and up This sets in motion an innate reflex whereby the self as a whole instead of firstly directly reacting to its environment indirectly firstly acts as a whole outwards on the environment in all directions in the greatest possible degree Thereby the integrative action of the central nervous system is given freedom to work at its best Thereby the person is provided with a unified whole self he may use for reacting to his environment with kinæsthetic information about his guidance of his actions working in the best way

Bolton, Lancs MUNGO DOUGLAS

ARGININE DEFICIENCY AND MALIGNANT DISEASE

SIR,—I noticed an abstract of a paper by D L Horrigan [1] reporting the excretion of uracil in 3 out of 5 patients suffering from myeloid leukæmia It occurred to me that there might be a possible connection between this observation and the finding [2] that the growth inhibition of a micro organism by uracil was prevented by arginine It may be that uracil encourages malignant change by suppressing the growth of normal cells rendered arginine deficient by the invading neoplasm, which then grows at their expense The simplest test of this hypothesis would be the administration of arginine in cases of experimental or human cancer

As a microbiologist I am not equipped to make tests, but some of your readers may care to co the possibility

Banstead, Surrey E J MILLE

REGISTRARS AND REGISTRARS

SIR,—I am a little surprised to read in your lett April 23 so embittered and venomous an epistle as signed by Registrar (W plus) The writer's ignorance military ranks *seems equalled by his lack* of know of teaching hospitals If by any chance he is likely become a "*failed registrar*" he may perhaps be ab take shelter under the Strachan umbrella

London, S E 1 J J CONYBEA

SIR,—Registrar (W plus) has raised a subject of interest to all registrars One point which req further stress in the inequality of duties is the fact the same difference in the amount of work done *registrars also exists in the teaching, but non profe* units

There are many registrars (W plus) working in tea hospitals—not only in peripheral hospitals, as correspondent suggests The group he describes as re trars (T) undoubtedly exists *in professorial units.* T add little or nothing to the every day (and night) run of a hospital service, but they use the time and facil to acquire further qualifications, and write nume papers On these achievements they are often elev *to consultant status in preference to registrars* (W with a wealth of practical and useful clinical knowle and experience

Of course, many of these experimental studies are considerable value, but it is unfair, with the ever incr ing expense of the National Health Service, that expanding number of hospital staff should be secluded *this type of work, whilst others of equivalent* st provide a 24 hour hospital service Clearly the pro time for writing theses for higher degrees and pub ing articles is when one has sufficient knowledge experience *to write with authority on the* subject *one's choice At the moment many higher degrees* obtained by men working in a laboratory on a su chosen and supervised *all through by their chiefs*, finally examine them Unfortunately in the keen comp tion for obtaining a consultant post, higher degree count, but in reality are these higher degrees of any clinical value? I doubt it!

REGISTRAR (W

PROTECTING THE MOTORIST

SIR,—There can be no doubt that in the near fu motorists will be more willing to use safety dev *against motor car accidents* Crowding on the r plus a high proportion of fast cars will ensure this

Most car accidents are preceded by a second or of warning During this period the natural reaction behaviour of most passengers can be imagined with description

May I propose the following emergency drill passengers, for consideration by *those* who h opportunity for experimental examination of the r or who have clinical experience of the type of inj in question? This drill is specifically designed to av injuries to the head and face when passengers are f *forwards against the windscreen*

The feet are raised and pressed against the d board or against the back of the front seat *in the* c of rear passengers The hands are cupped under t chin, the elbows being wedged in the groins This w prevent whip lash strain of the neck

If this method were to gain medical approval, it ma be possible to include it in the *Highway Code*

Hornchurch, Essex I H J BOURNE

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[1] *J clin Invest* 1954, 33 901

[2] *Nature, Lond* 1950, 166, 1035

MEDIAN-NERVE PALSY AND ACUTE INFECTIONS OF THE HAND

SIR,—May I add a similar case to those described by Bailey and Mr Bolton Carter in your issue of rch 12? It is one of 42 cases of carpal tunnel syndrome ated during the last four years, upon which a report now being prepared

A butcher aged 49 was seen on July 7 1953 with a pulp ction of the right thumb which had been drained two s previously He had had systemic penicillin for one y before incision and for the next two days, and this was tinued He had much pain in the hand and wrist avated by extension of the fingers, which were held in the ition of rest Movement of the middle and ring fingers greatly restricted the index and little fingers less so e thumb could be moved more freely but this caused some n. Pain at rest was in the median nerve distribution l was severe enough to keep him awake There was tender s on the palmar aspect of the hand over the carpus and t joint with diminution of sensation of light touch but pin-prick over the median nerve distribution in the hand. dorsum of the hand was considerably swollen.

For the previous eighteen months he had had pain in right hand with acroparaesthesiae in the distribution of the dian nerve every Friday night which had repeatedly ken him. On Saturday mornings the hand was stiff and b with limited finger movement and some residual gh lessening pain this subsided completely by midday Saturday not to recur until the following Friday night. se symptoms had become progressively worse until he had ely been having pain on occasional nights during the week ficient to awaken him (Butchers are busy in South tralia on Fridays, because they have to prepare large ers for the weekend for a population that eats a lot of at and they do not open on Saturdays.)

In spite of continued penicillin and rest in a plaster back b with elevation, the hand grew steadily worse the fingers re immobile and their movement more painful, until lly he could have no finger moved passively into extension hout great pain Sensation loss by July 11 was complete light touch and much impaired to pin prick over the median ve distribution. Tenderness at the wrist was much reased.

Decompression of the median nerve was therefore done July 12 by longitudinal incision through a convenient mar crease The flexor retinaculum was divided fully nerve was found to be swollen and reddened in the ximal half of the carpal tunnel and relatively narrowed dark red in its distal half A little serous fluid was present there was no abnormality of the tendons. The skin was rly sutured and it healed well Convalescence was slow satisfactory He was back at work in four weeks, although ory loss and strength of the hand did not recover fully four months.

On April 18 1955 he said that he has had no trouble since, hand has remained normal, and his working capacity is mpaired The scar is supple pain free and hardly visible

I feel little doubt that the infection caused an inflam tory swelling in the carpal tunnel which converted a odic occupational carpal tunnel syndrome into a ative emergency I think it probable that Mr Bailey d Mr Bolton Carter's cases fall into the same category

In case 1 there was a history of rheumatism in the ds which may well have been a carpal tunnel syndrome d they mention osteo arthritis in the left hand, which in the es may be a factor in the production of the syndrome case 2 there is no mention of previous history but it is possible that inquiry might reveal that the patient d previous symptoms of median nerve compression Both these patients fall into the age and sex group most commonly cted by carpal tunnel syndrome—i.e., women at or out the time of the menopause Case 1 had been having ptoms for years and these probably first arose at the time the menopause.

In both of these cases the early and marked loss of sensation is particularly interesting As well as the butcher I have en it in one other patient—a man with a severe carpal jury and projection of part of a fractured lunate into the pal tunnel His flexor retinaculum was divided and the jecting bone removed three weeks after the original injury but by that time he had complete anaesthesia over the median nerve distribution in the hand which took six months to recover There was acute tenderness over the median nerve at the wrist but apart from some loss of finger movement by mechanical interference, there was little motor impairment.

The restriction of finger movement in all these cases must be due to mechanical interference in the carpal tunnel by compression of the tendons. The dominance of sensory loss seems to be a feature of the more acute lesions in the usual and much less acute carpal tunnel syndrome wasting of the thenar eminence and weakness usually come before definite sensory loss Such patients, however often complain of numbness at the finger tips, especially in the early morning which interferes with knitting and sewing

I agree with Mr Bailey and Mr Bolton Carter that the compression in their cases was the result of inflammatory exudate and consequent ischæmia of the median nerve, but I think that there was a pre-existing lesion which narrowed the carpal tunnel, predisposing to the nerve compression This may in some cases be a stenosis comparable to De Quervain's disease or some other factor possibly hormonal but whatever the predisposing factor the median nerve lies in the carpal tunnel in a particularly vulnerable position In none of my cases has any disability resulted from division of the flexor retinaculum This is not surprising in view of the fact that all strong movements of the human hand occur with the wrist in extension The flexor retinaculum in man seems to be a useless structure

I was interested to read that Mr Bailey and Mr Bolton Carter required a longitudinal palmar incision to be sure of adequate exposure and division of the flexor retinaculum I have tried the transverse wrist incision found it inadequate and reverted to the longitudinal. There are objections to this incision, but in practice they all heal rapidly and well with no disability, especially if carefully made in a crease.

As soon as the diagnosis of median neuritis from compression has been established I make it a rule to divide the flexor retinaculum as soon as possible to avoid the chance of irreversible damage to the nerve. The only exception to this rule is in menopausal women with mild symptoms, which may sometimes be completely relieved by œstrogens. But should there be no improvement within a short time the rule still applies

Royal Adelaide Hospital
Adelaide South Australia.

J D SIDEY

IRON DEFICIENCY ANÆMIA IN PREGNANCY

SIR,—The question of iron therapy in pregnancy is a topical one and articles such as that by Dr Gatenby and Dr Lillie in your issue of April 9 are very helpful in dealing with the practical aspects of this subject

May I make one or two comments on points made by them? It is true that there is a high incidence of intolerance to the ordinary ferrous-sulphate tablets but I have hardly ever found intolerance to enteric-coated ferrous sulphate tablets, so it is to this form of therapy I turn when the former fails. The enteric coated tablet costs only about double the ordinary variety Ferrous gluconate, however I am told costs about ten times as much as the simple ferrous-sulphate tablet This may be worth considering It is true that some might argue that there is a danger of the enteric-coated tablet passing through the gut undissolved especially as the ordinary tablet passes a long way (as demonstrated radiologically) However the clinical response appears to be adequate, so I am not unduly disturbed by this

Another point is in connection with parenteral forms of iron therapy, so widely used now Why should an anæmia discovered late in pregnancy be an indication? All the evidence I have seen shows that the response to oral iron should be as quick as to parenteral iron[1] A quicker response, then, cannot be claimed If one ensures that the patient can take, and is taking, her oral iron, by asking her a few days later, then intolerance of oral iron is no argument Finally, I believe that a form of iron-deficiency anæmia which fails to respond to oral iron is very rare indeed Most of these cases will prove to be megaloblastic if a sternal marrow examination is made

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[1] Jennison R F Ellis H Lancet 1954 ii 1245

St James's Hospital
Leeds 9

T F REDMAN

MADE-UP WORDS

SIR,—" Bibliotherapy " indeed[1] ! How long are we to tolerate this pompous, humourless, self-important use of long made up words to describe such a simple procedure as providing helpful books for a child or his parent to read ?

Institute of Diseases of the Chest
London, S W 3

J G SCADDING

RADIOLOGY OF PLACENTA PRÆVIA

SIR,—Dr Blair Hartley is doing excellent work in using his special technique for visualising radiologically the *calcified* placenta in localising its position This, he told us in his letter of last week, he can do in rather less than 1 in 3 cases Just in case there are some, among the many who I hope will read his letter, who have not yet been sufficiently convinced of the undoubted merits of ordinary soft-tissue placentography to take it up, I feel I must reassure them that it is quite unnecessary for calcification to be seen in order to determine the placental position

Dr Blair Hartley says that seeing the calcified placenta is factual evidence , agreed, but it would be a pity if those still hesitating to adopt soft tissue placentography became so disappointed at their failure to *see* the placenta in over two thirds of their cases that they did not finally adopt it and thus denied to themselves and their patients the great advantages of the method

The London Hospital, E 1

ROBERT PERCIVAL

FUNCTIONAL SYMPTOMS IN ORGANIC DISEASE

SIR,—In the final paragraph of Dr Barham Carter's somewhat breezy article last week, there occurs this sentence " The great tragedy, of course, is to miss the organic "

It is surely sad that in 1955 it still needs to be pointed out that this attitude reveals a long out dated overvaluation of the soma, and that the tragedy of missing the psychogenic is neither less nor greater but exactly equal to the tragedy of missing the organic

Thirteen years ago an article appeared in *The Lancet*[2] entitled Neurosis Simulating Organic Disorder This dealt with 50 cases which had been referred by Army doctors to an E M S hospital with a definite diagnosis of organic disease, and in which the condition was ultimately found to be purely psychogenic Any case in which even the suggestion of nervous disorder had been raised was excluded from the series

34 of these patients had been admitted to the medical and surgical wards, and constituted 20% of the hospital intake for the 3 months covered by the investigation ,

8 of these patients had spent between them 96 weeks in various hospitals and 106 weeks on light duty ,

19 of these patients had between them been radiographed 30 times, including 12 barium meals, 2 barium enemas, and 2 intravenous pyelographies ,

7 of these patients had received physiotherapy totalling 35 weeks' inpatient and 56 weeks' outpatient treatment

All this staggering waste of professional time and public money was not merely useless to these patients, but actively harmful to them in that it confirmed original fears that they had some serious organic di In many cases it probably made them ther inaccessible to psychotherapy and condemned to a of invalidism

I suggest that this also is a tragic issue I s that while both these types of medical error are tr " the great tragedy " lies in the lack of that bala psychosomatic approach which would make a do as ashamed of missing a psychogenic disorder as he is of missing an organic one

London W 1

ALAN MCGLASH

MASKED EPILEPSY

SIR,—I have closely followed the arguments in rel to Dr Wallis's paper of Jan 8 If one agrees that in the leg, cyclical vomiting, headaches, pyrexia, abdominal pain are fairly common manifestation epilepsy, how far does this help in the treatment ? these cases the forerunners of Hallhuber's autono dystonias,[1] or the "*Manager-Krankheiten*" of the generation ?

I agree with Dr O'Neill (April 2) and his tension the These cases need more than phenobarbitone Bu exploration of the child's mental state and his envi ment must take too long and there are too few psy therapists I look forward to controlled research hypnotherapy Tension appears to be rapidly destro and the child is defended against himself As Bram says[2] " He becomes more in control of his organism."

London, W 1

GORDON AMBROS

SANATORIA

SIR,—I read Dr Edwards's letter last week interest While agreeing to a large extent with wha says, I think there is one factor he has not mention namely, that it is quite possible that in the near f patients will refuse to go to sanatoria many miles d from their homes

As regards teaching tuberculous patients " to with their disease," I would say that diabetic pat learn to live with their disease very satisfactorily wi having to go to special institutions for the pu Nevertheless, I quite agree that there is still a plac sanatoria in the treatment of tuberculosis, provided are near the centres of population that they serve.

Hastings

A W ANDERSO

THE DIFFICULT APPENDIX

SIR,—Every young general practitioner should the article by Mr Kerr in your issue of April 9, w reveals the many difficulties in such a common diso and older readers may be consoled over their failures, either in not operating soon enough or in rem ing a normal appendix Two of my own cases may th some light on our difficulties

One hot summer a 7 year old boy suffered from indig and diarrhœa He was still playing with his friends be he had no fever, pain, or vomiting, till sent home by an mother because he was incontinent of liquid fæces He put to bed by his doctor, who was told about generous of unripe apples Bismuth was prescribed Three days la though not complaining of any pain, he was admitted to pital suspected of salmonella infection (leucopenia splenomegaly, and diarrhœa) In a couple of days he se to improve He had neither fever nor pain, but a leucocy developed A surgeon concluded that there was no sur cause, and that the condition was probably paraty That night the boy collapsed with upper abdominal pain rigidity, black vomit, and meteorism A perforation suspected and the abdomen was opened, but a gangre rocæcal appendix and an abdomen full of pus was found boy died three hours later

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[1] *Lancet*, April 23, 1955, p 858
[2] Cook, G T, Sargant, W *Ibid* 1942, i, 31

[1] Hallhuber, M. J *Ars Medici, Liestal*, 1953, 43, 462
[2] Bramwell, J M Hypnotism. London, 1930

6-year-old girl complained of colic and vomiting Her perature was slightly elevated No typical muscular nce could be found in the abdomen but by palpating ply in the cæcal region some resistance was noted The endix was removed but it was only slightly red No hological examination was made. Her general condition riorated with continuous vomiting meteorism, and r When I first saw her the child was seriously ill with ched nose acetonuria, and leucocytosis (23 000 per c.mm h shift to the left and toxic granulations) X ray examina of the chest showed that the diaphragm was high moved poorly but there was no other abnormality An avenous drip of glucose-saline solution followed by plasma ed time for arguments to be considered in favour of ning the abdomen Within two hours the child underwent arvellous change; no vomiting no fever less meteorism. view was that this was a case of cyclic vomiting with tonæmia. Within a week the child was discharged fectly fit

Hilversum. D P R KEIZER.

POLIOMYELITIS VACCINES

ir,—The Salk anti poliomyelitis vaccine is prepared n monkey tissue cultures Is it certain that injection this preparation will not produce rhesus antibodies en injected into susceptible human subjects, most ecially those already sensitised ?

estminster School of Medicine
London, S W 1 J G HUMBLE

RUPTURE OF LAPAROTOMY WOUNDS

ir,—In reading Mr Standeven's article of March 12 l the subsequent correspondence I have been struck the lack of reference to what I believe to be a most ortant feature I have re sutured over 30 burst domens and in all cases I have noticed the firm erence of part of the prolapsed bowel or omentum the edges of the peritoneum and the subcutaneous ues. Surely this suggests that some part of the peritoneum has given way at an early stage Small gut or ntum protrudes and lies just deep to the skin itoneal fluid escapes and (I believe) delays healing the superficial layers When the skin stitches are oved the whole wound disrupts and more bowel may n prolapse

r Standeven and Mr Walsh (March 26) rightly s the significance of the serous discharge In my erience this always indicates an impending rupture ach cases inspection and percussion may demonstrate t small bowel lies just below the skin

believe that the most important layer of the ominal wall is the peritoneum Unfortunately it is the akest If the patient is straining at the time of its ure the peritoneum may split at right angles to line of suture In several cases I have found the ure line to be intact but bowel escaping just lateral it

doubt if the incidence of dehiscence of laparotomy unds is in any way influenced by such general factors anæmia or protein or vitamin deficiency—or even al sepsis. If the peritoneum stays intact there will no burst abdomen I feel therefore that Mr andeven s distinction between early and late ruptures an artificial one If the skin stitches are left in till te the skin edges will probably hold The later a rst abdomen occurs the more difficult it is to separate it of the bowel from the subcutaneous tissues

In my own experience I have found that :

(1) Transverse or oblique incisions are less likely to rupture an vertical ones because the pull of the abdominal muscles es not tend to separate the peritoneal edges

(2) The abdominal wall must be relaxed until peritoneal sure is complete

(3) Nylon is unreliable

(4) Short ends of knots must be left long and the gap between stitches kept short

(5) The peritoneum is less likely to split if a horizontal mattress suture is used

The London Hospital, E 1 A J WALTON

SIR,—Like other correspondents, I found catgut and monofilament nylon unsafe in suturing the rectus sheath Interrupted thread and silk was secure but tedious to insert For three years now I have been using continuous braided nylon (Finlayson's *no 6 green*) It is pleasant to use and so far safe Although there have been some infected wounds it has only once been necessary to remove the suture

Braided nylon has more elasticity than monofilament nylon so should be less likely to cause the tight feeling in the wound mentioned by Mr Oldham (April 16) This *sensation* has been *mentioned* by *only* one patient but has not been asked for specifically so may well be more common Certainly the knots are unobtrusive

London W 1 A. M DICKINS

HYPOGLYCÆMIC EFFECT OF DIMERCAPROL

SIR,—Concerning the preliminary communication by Dr Butterfield in your issue of March 5 the papers on sulphur and diabetes mellitus published by Prof Andreu Urra and myself from the medical clinic of the University of Seville are perhaps unknown in Britain These papers were based on a series of experiments which are the subject of my thesis on the problems of sulphur and uric acid in diabetes mellitus[1] Professor Urra and I have also published another paper on sulphur and the metabolism of glucosides in diabetes mellitus.[2] In these investigations low levels of glutathione were usually found in diabetic blood and experimentally alloxan diabetes was prevented by giving preparations of sulphur We treated diabetics with dimercaprol and found only a slight tendency to reinforce the action of insulin and hyperglycæmia and glycosuria improved

Seville MIGUEL RIOS MOZO

BURNS FROM ELECTRIC BLANKETS

Mr F Grisley B.SC managing director of the Warm Glow Co Ltd , writes :

In your issue of April 2 Dr Neville Davis reports an accident with an electric blanket To avoid risk of accidents the manufacturers normally instruct the user to switch off the blanket before getting into bed but people often disregard this advice Alternatively a waterproof sheet may be used between the blanket and the sleeper This also may be disregarded, or a worn or pervious sheet used with disastrous results. The use of an earth as suggested by Dr Davis, is impracticable and even dangerous for the blanket should be an earth free appliance with no exposed metal parts.

In 1948 my company introduced a plastic-covered waterproof element into all our blankets. This not only prevents danger from bed wetting, but it also enables the whole blanket to be immersed for laundering The plastic covering used is stable and flexible, and lasts indefinitely This particular kind of accident therefore need never occur

PLASTIC APPLIANCES MOULDED DIRECT TO PATIENT

Mr R A E. Walker secretary of the National Research Development Corporation writes

In his article of April 23 Dr Brennan refers in a footnote to patent application no 16668/51 It may not be clear to your readers that this application relates to the proposals communicated to us by Dr J T Scales of the Institute of Orthopædics Royal National Orthopædic Hospital Stanmore for the preparation of composite material of Polythene (polyethylene) and Moltopren (polyurethane) and the moulding of surgical splints therefrom by application to plaster casts or directly to the patient The patent rights in Dr Scales's invention have been assigned to the Corporation for exploitation in accordance with the Development of Inventions Act 1948 Application may be made to the Corporation for further particulars.

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1 *Hisp Med* (in the press)
2 *Folia Clin Internac* May 1953 no 5

Obituary

EGBERT COLEBY MORLAND

M B, B Sc. Lond, M D. Berne, F R C P, F R C S
EDITOR OF THE LANCET, 1937-44

In the development of a journal a few men and women play outstanding parts The influence of Dr Morland's original mind and new points of view was apparent from the time he joined the staff of *The Lancet* in 1915, and it continues through those he taught

In few ways an ordinary man, he brought to his main task a knowledge and experience as unusual as it was useful

He was born on Sept 3, 1874, the fifth son of Charles Coleby Morland, J P, of Croydon, and his wife Jane Fryer The Morlands and the Fryers were Quakers from the North of England, and the Croydon family was both brilliant and unconventional Egbert, a clever but uneasy boy, was sent to the Whitgift Grammar School and then to Bootham, the Friends' school at York A taste for science was confirmed by a period at Owens College, which also gave him a lifelong bond with Manchester He took his B SC with first-class honours in zoology, and went on to St Bartholomew's Hospital with a senior scholarship At Barts he won the Matthews Duncan prize and was vice president of the Abernethian Society, and after taking the London M B in 1898, with the gold medal in physiology and honours in anatomy and organic chemistry, he became successively ophthalmic house-surgeon and house physician at his own hospital, and house-physician at Wolverhampton General Hospital His next appointment, in 1901, was at Great Ormond Street, and it was then that the natural sequence of his career was rudely broken He developed tuberculosis

Like many another medical victim of this disease, he presently found himself making it his special study The first fruit of this new interest was an essay on the design of sanatoria, entered for an international competition held in 1902 before the King Edward VII Sanatorium was built at Midhurst There were 180 competitors, and with the aid of his architect brother Morland gained third prize for his plans, which were published in the first issue of *The Lancet* for 1903 The new phase in his life was soon established, for after living for a while in Switzerland to recover his health he decided to remain and make his home in the mountains In 1903 he married Mary Windsor Latchmore, a woman of zest and character who helped him devotedly till her death in 1948, and when he had taken the Swiss Federal Diploma they settled at Arosa, where he practised in three languages and from 1907 to 1914 directed the Villa Gentiana, an English sanatorium In 1905 he was writing in these columns, with W R Huggard, on the action of yeast in tuberculosis and its influence on the opsonic index, and his M D thesis at Berne in 1907 was on *opsonins—a subject then in the bacteriological forefront* From the German he translated Turban's *Diagnosis of Tuberculosis of the Lung* and Bandelier and Roepke's *Tuberculosis in Diagnosis and Treatment* In 1913 he produced a small book, written with Clive Rivière, on *Tuberculin Treatment*, and a paper on technique of artificial pneumothorax

This phase was ended by the outbreak of war, and next began almost by chance Now some 40 years he left Switzerland to join in the Society of Fr relief work on the Marne Before doing so, however, had displayed his journalistic talent by abstracting *The Lancet* a statement by Paul Eltzbacher on food supply of the German people, and when twenty-column contribution arrived one day ju the journal was going to press, the editor had paid compliment of holding back the week's issue until it be included When Morland returned to London the Marne and called at the old *Lancet* office at the co of Bedford Street and the Strand, Sprigge wa difficulties because Gerald Horner, then *assistant ed* was serving in the R.A M C, so he said to Mo "why not stay and help?" And Morland sta for 29 years

At this point one might follow the precedent of Hebrew biographer who referring his readers to the of the Chronicles of the King Israel and Judah But though bound volumes of *The La* since 1915 contain most of acts of Morland, and would been very different without what he did himself is inextrica mingled with what other peo did In an effort to analyse influence it has been truly that he found the journal hum but left it human, but perh his greatest effect on our colu was one of refreshment He this effect because he was *artist* and (to the end of unexpectedly long life) a petually surprising person

The artist enables people to familiar things anew, and land had just this faculty angle of vision always seemed be a little different, and, th *this often embarrassed and* s times alienated his acquainta it helped him to be not only an animating journ but an exceptionally valuable member of our profess for to look at things at a new angle is often hig instructive He also had the catholic curiosity of investigator and was ready to be thrilled by any fr thought or fact—though he might lose interest quickly When he wanted to do so, he could absorb body of knowledge very thoroughly, and he rememb a great deal about a great many diverse subjects, fr mathematics to midwives, from infant feeding to European flora, but he had little intellectual taste generalisation, and tended to look at one thing at a ti "on its merits" Hence, as an artist, he preferred small canvas to the large one, and he enjoyed paint detail But whether the canvas was large or small, would avoid monotony by an engaging touch inconsequence in the composition

If this is not the portrait of a creative thinker, it nevertheless the portrait of a born journalist, born make others think Moreover, in this delicate and of exhausted man—the "old poitrinaire" as he cal himself—the mental liveliness was matched and ma profitable by an astonishing capacity for work, day day out, year in year out Skimming, as it seem through the millions of words that poured into th office, he could quickly detect what was new and intere

Morland, when he wanted, could write so catalytic a letter as to draw a contribution from the most unreactive of experts, and even his routine communications were carefully written in a personal way—often in fact by hand But it cannot be said that even through the post he wholly satisfied everybody, for ordinary people often prefer ordinary letters, and few besides harassed editors know how correspondence may improve if allowed to "mature" Those who went to *The Lancet* oracle with a question must be prepared for an oracular reply, which left the "onus" (to use another of Morland's favourite words) on the person receiving it The following, for example, is his answer to a long letter from a doctor who wanted to know about the copyright regulations governing the reproduction of *Lancet* material in foreign broadcasts

Dear L,

I am glad to hear you are helping the British Council to let South Americans know what British medicine is doing We do our own bit too I don't feel I can give you any general guidance on copyright in the air But you would find the Golden Rule applicable and between ourselves the Hippocratic Oath is binding

With kind regards, Sincerely Yours,

EGBERT MORLAND

Copyright was one of the subjects that did not interest him

Even his colleagues seldom had their questions answered directly or comprehensively But when his mental processes seemed to be at their most devious and detached the probable reason was that he was not yet ready with his decision, which he would give in his own time and his own way It was partly because he was so puzzling that he was so fine a teacher, and, whether amusing or infuriating, his enigmatic instructions somehow extracted from his juniors the same kind of effort that he himself put into *The Lancet*

Nor did this taste for the oracular prevent his being energetically practical in other fields when something within his compass needed to be done Hence in his spare time (which did not exist) he did solid work in many useful causes, and in various ways he was of service to the Queen Alexandra Sanatorium at Davos, to the Enham (now Enham Alamein) Village Centre for Disabled Ex Servicemen, to the Medical Defence Union, to the Society for the Relief of Widows and Orphans of Medical Men, and to Sibford School, of which he was a governor But, though a good speaker, he seldom appeared on platforms or at the meetings or dinners of medical societies Disliking public occasions, he was inclined to think that an editor should be a back-room boy, neither seen nor heard except through his journal, and invisible especially to callers None the less he was a sociable person, and never more happy perhaps than in the Athenaeum, which likes a proportion of its members to have their eccentricities He was happy, too, in the fellowships conferred on him by the Royal College of Surgeons in 1936 and the Royal College of Physicians in 1941, though both colleges probably wanted to withdraw their honours when they saw that he described himself (whether to save space or out of modesty) as FRCP&S

When Morland succeeded to the editorship in 1937 he was already 62, and two years later, when war broke out and the decision was reached to move the journal out of London, he was tempted to resign his sisyphean task But, as it turned out, the move to Aylesbury proved a tonic Settled cosily in a flat above the tiny office in Temple Street, he abandoned even the convention of office hours and did most of his downstairs work after supper when his juniors had gone home Freed from the social obligations of his chair, and disguised from former friends by a beard and a dilapidated mackintosh, he took an eager interest in the war-time life of the small market town, and spent more of his time in reflection and reading—though even now he never finished a preferring the random sample With a senior's less of inhibitions, he was finding it easier to show abundant kindness of heart and concern for oth but to keep the balance he showed also more of sharpness of his tongue When directed towards rather than individuals, this asperity was gre enjoyed, and it is pleasant to find in our files his de comment on a rather pompous declaration in distinguished signatories defended the rights and of the citizen Underneath, in his small, neat, decor hand, Morland has written

* I'd rather be in prison with my friends th
free with that lot. Ed. L.

It was sad, in a way, that he should not take com of his journal until his most active years were for he never got full credit for his achievements, these were different from what they might otherwise been But possibly *The Lancet* did not lose the for in his more impetuous moments he often nee someone to tell him to think again Moreover, tho he could rule both by love and by fear, he was not a commander he was a prophet or priest rather th king—an impish prophet but in direct line from the Testament During the war he was already an old with the defects of his high qualities becoming apparent, and it was inevitable that in his cour Aylesbury the executive responsibility should dev more and more on his lieutenants—as once it devolved from Sprigge to him So the honou burden was partly transferred to younger shoulders, when *The Lancet* returned in 1944 to London Mor retired into private life—with a characteristic valedic greeting to his readers

At first at Aylesbury, and afterwards in an old house beside the ancient Friends' meeting hous Wooldale in Yorkshire, he adjusted himself yet aga new circumstances He had given much thought to age—its disabilities and possibilities—and had been one of the first to see the need for a con movement for old people's welfare, comparable complementary to the movement for infant welfare developed during and after the previous world war 1945 he expressed his ideas in a charmingly Morlan pamphlet called *Putting Them on the Map*, written Buckinghamshire committee of which he was instiga member "We must search out the old people in hidey-holes," he said, "and find for ourselves whe they are content with their lot, whether it is a lot which they should be content, and if not what we sh do to amend it" Himself, he well understood the of continuing to be active, and as lately as 1951 he w the biography of a pioneer midwife, entitled *Alice and Stork* He had the advantage of being one of those wh pleasures are of the mind, and for some years of retirement he was also fortunate in his keen enjoym of gardening and walking, and in the companionship his wife But each in turn was taken from him, eventually almost all the power of sight By refinement of age, and its distresses, his face bec less that of a prophet than a saint—a rôle to which had never aspired One of his chief hopes, he said that he might continue to amuse those around him.

He died at York on April 26, in his 81st year, even to the last his mind, though wayward, reta the ardent quality that so often made him seem youngest, though maybe also the oldest, of his comp Throughout his life he belonged to the present and future rather than the past, and many who knew as well as many who did not, have cause to be grat for his disturbing, enlivening, and enlightening spirit

WILLIAM BURRIDGE

D.M. Oxfd

Dr William Burridge formerly professor of physiology l principal of the King George's Medical College and n of the faculty of medicine at Lucknow University d in hospital at Dartford, Kent, on April 21, at the of 69 He was the author of *Excitability a Cardiac dy* (1932) *A New Physiology of Sensation* (1932) *New Physiological Psychology* (1933) and many short les in various journals.

T B writes 'Like his fellow Cornishman mphry Davy, and his pupil Faraday Dr Burridge de important discoveries through brilliantly original eriments using very cheap and simple apparatus book *Excitability* describing his experiments on frog's heart is a medical classic, and this study the beating heart's responses to stimulation enabled to correlate similarities in nervous action and con ous sensation to deduce rhythmical activity in brain l spinal cord neurones and in sensory end-organs and elaborate many logical consequences of assuming ythm in neurones. The fact of rhythm in cerebral rones has since been independently confirmed by er workers some of his predictions remain to be ved by experiment.

"So far Dr Burridge's work has not received the eral acclaim it deserves. We owe to him the new d revolutionary concept of responsiveness as distinct m excitability, a new method of research in pharma ogy, giving new and surprising information on the ltiple actions of some drugs and their quite different ects in large and small doses and a new physiological chology harmonising experiment, sensuous experience d deductive reason and well in advance of any previous ory of sensation and of thinking process.

His own explanation of the opposition that his work d theories met was the power of an orthodox primary umption to blind fully organised minds to any new th that contradicted teaching elaborated from the mary falsely generalised preconception His Puck ing the Doctors (*Medicus* December 1952) gives a l statement of his defence and repays reading

PATRICK KERR DIXON

M.D Dubl. F.R.C.S.I

Dr Patrick Dixon who died on April 21 at Lusaka rthern Rhodesia, had spent nearly thirty strenuous and enturous years as a medical missionary in the Belgian ngo.

e was born in 1898, the son of the late Andrew on, professor of anatomy and dean of the school of ic at Trinity College Dublin Patrick's studies Trinity College were interrupted by the 1914–18 and he was mentioned in despatches for services h the Royal Garrison Artillery in France In 1918 returned to Dublin to graduate in 1922 in science, h first-class honours in mathematics and experimental ence. Two years later he graduated M.B with honours. In 1926 he joined the Garenganze Evangelical Mission the Belgian Congo

For the next twenty five years, despite the effects of ere injuries sustained when he was mauled by a lion, he ved the people of the Luapula Valley with devotion the course of his work he saw the suffering caused by choma and in 1929 he visited India to study this ease under Sir Henry Holland. His published work ls with his experience of its treatment in Central Africa. e hospital which he founded at Chibambo became a ntre for the treatment of eye diseases. In recognition of services he was decorated by the King of the Belgians. In 1952 ill health forced him to leave the Luapula alley, and for a time he was medical officer at Nkana he In 1953 he joined the staff of the Government frican Hospital at Lusaka He also taught at the frican Medical School

A colleague writes: 'Pat Dixon was an eager tireless l devoted worker, content to make do with the most agre equipment yet keeping himself up to date in the dical world and always looking forward In this he as a true disciple of the great Dr Livingstone who had rsed the same country fifty years before Like him o, Dixon bore to his dying day the marks of the lion's unch in his left humerus. He will long be remembered on the divide between Congo and the Zambezi watersheds'

His first wife, Miss Olive Arthur died in 1927 In 1934 he married Miss I H Russell who survives him with a *daughter of his second marriage*

KENNETH BENSON BELLWOOD

O.B.E., B.A, M.B Camb., F.R.C.S.

Dr Bellwood consultant surgeon to the ear nose and throat department of Bedford General Hospital, died at his home on April 17 at the age of 64

He was born in Middlesbrough and was educated at Coatham School, Redcar He was a scholar of Pembroke College, Cambridge, where he took the natural sciences tripos in 1912, and a Shuter scholar at St. Bartholomew's Hospital qualifying in 1914 During the 1914–18 war he was appointed O.B.E. for outstanding service in the Royal Navy In 1917 he took his M.B Soon after he returned to civilian work he entered general practice in partnership with the late W H Miller in Bedford and also specialised in diseases of the ear, nose, and throat. In 1921 he obtained the F.R.C.S. When in 1930 he was appointed E.N.T surgeon to the Bedford County Hospital he laid the foundation of the present successful large and busy E.N.T department at the Bedford General Hospital Despite ill health which first showed itself in 1940, he worked indefatigably, and he was appointed consultant surgeon to the department when the hospital was taken over by the National Health Service in 1948

G A M writes: 'Dr Bellwood as he is called by all in Bedford was loved for his quiet modesty and great kindness to all his patients The greatest sorrow will be felt by the patients he looked after as a general practitioner He loved the hills, and was a great walker in his day Even when he could no longer climb he always went north to his beloved Yorkshire for his holidays'

In 1921 Dr Bellwood married Florence Violet Cooper, who survives him with two daughters

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Appointments

BELCHER J. R., M.S. Lond., F.R.C.S., M.R.C.P.: asst. thoracic surgeon Middlesex Hospital London

DAWES J D K M.D Durh F.R.C.S. asst consultant surgeon E.N.T department Royal Victoria Infirmary Newcastle upon Tyne and surgeon to the Newcastle upon Tyne H.M.B

GRIFFITHS E. P M.R.C.S D.OBST D.C.H asst M.O.H., Gloucestershire

MATHER, J F M.B Durh: school M.O Newcastle upon Tyne

MILLS, W G, M.B. Birm F.R.C.S., M.R.C.O.G part time consultant obstetrician and gynaecologist, mid Worcestershire group Birmingham R.H.B.

SKONE, J F M.D Lond., D.C.H D.P.H D.I.H M.O.H., chief welfare officer and principal school M.O., West Bromwich.

South-Western Regional Hospital Board:

LEAHY T C, M.B., N.U.I S.H.M.O Hortham Brentry hospital group Bristol.

WALKER, W I M.B Aberd D.P.H, D.P.M medical superintendent Hortham Brentry hospital group

WALLEY R V, M.B. Camb deputy resident physician Ham Green Hospital near Bristol

Manchester Regional Hospital Board:

HOYLE THELMA B, M.B. Manc., D.A asst anaesthetist (S.H.M.O) Burnley and district hospitals

KIRBY J R, M.B Leeds D.M.R.D consultant radiologist Wigan and Leigh hospitals

O REGAN JOHN M.B., N.U.I, D.P.H tuberculosis physician (S.H.M.O) Preston and Chorley hospitals

Liverpool Regional Hospital Board:

JONES, C H., M.B. L'pool: whole-time asst. pathologist Alder Hey Children's Hospital Liverpool

RICHARDSON J C M.B. L'pool F.F.A R.C.S. D.A consultant anaesthetist Liverpool city area.

WALKER G D D.M Oxfd M.R.C.P consultant physician superintendent Newsham General Hospital Liverpool

WALLACE JONES, D R., M.B. L'pool D.M.R.D consultant radiologist North Liverpool and Fazakerley groups

The Hospital for Sick Children, Great Ormond Street, London:

BAILLIE R C, M.B. Lond house-surgeon orthopaedic and plastic departments

JOHNSTON W H M.D Toronto: asst medical registrar

SMITH, ISABEL G M.B Lond., D.C.H house physician

TODD J I M.D Toronto F.R.C.S D.C.H: part time surgical registrar

WYLLIE, G G M.B Adelaide F.R.C.S.: resident asst surgeon

East Anglian Regional Hospital Board:

CHATTIN F M M.B Lond M.R.C.P: physician-superintendent Papworth Hospital

GILLIE, ALEXANDER, M.B Glasg asst psychiatrist Little Plumstead mental-deficiency group of hospitals and child psychiatry service

MARTIN W M M.B. anaesthetic registrar Newmarket General Hospital

WELLS J M WESTON, M.R.C.S. D.M.R.D consultant radiologist, King's Lynn and Wisbech area

Notes and News

HEALTH EDUCATION

At the seminar for public health workers organised by the Central Council for Health Education of Great Britain and held in London from April 19 to 23, delegates attended from 21 countries Dr W Emrys Davies, education officer to the council, said that people do not listen to instruction unless they feel that the subject matter is relevant to their own problems and way of life Hence the first task of the health educator is to assess the basic human needs common to all, in any country, whatever the conditions or climate The second is to establish an atmosphere in which discussion can flourish, and experiments have shown that the discussion group can achieve what its members could not achieve singly The group leader is therefore a more effective person than the lecturer talking to an audience and isolated from his hearers by natural barriers of platform position, shyness, and absence of communication of ideas between members of the audience Dr John Burton, medical director of the council, described the use of case histories which command interest from members of a group and which recall to many experiences that can be used as a basis for discussion Mr W Sellers, film adviser to the Colonial Office, said that in dealing with illiterate people one must evolve three dimensional visual aids which come within the range of their everyday experience Diseases have to be classified in relation to their causes and source—e g, insect infections, airborne and water borne diseases In Nigeria a film van has proved a big attraction because people will comprehend a moving picture when the still one makes no impression

UNDERGRADUATE TEACHING IN LONDON

The difficulties of undergraduate teaching hospitals arising from the shift of population from the centre of London are mentioned by Colonel J J Astor, chairman of the board of governors of the Middlesex Hospital, in the hospital's statistical report for 1954 At the Middlesex the bed occupancy rate is over 90%, and the pressure on the outpatient department is as great as ever, but "there is a tendency for clinics and wards to be deprived of various types of case which are valuable for undergraduate teaching Patients suffering from these conditions are now for the most part being treated at hospitals in the peripheral areas, and in consequence medical students of today are not seeing the cross section of illnesses which was available for their predecessors when this was still a residential area" As an interim measure the Middlesex has arranged with the Luton and Dunstable Hospital for some of the patients on that hospital's waiting list, with their consent, to be transferred to the Middlesex for treatment, and this scheme is working well

"THREE MEN"[1]

Miss Jean Evans, a writer who has turned her talent to presenting the case histories of three living men, describes her book in a sub title as "an experiment in the biography of emotion" Johnny Rocco began life as a rejected child who was often delinquent, but who has finally made a precarious social adjustment William Miller, too, was often delinquent till he became blind, he recovered his sight but (perhaps finding the responsibilities of sight too heavy) became delinquent—and blind—again. Martin Beardson is a tormented homosexual She tells their stories with sympathetic insight, but without interpreting the psychological mechanisms at work. It was inevitable that she should select, from the vast quantity of material she has amassed in the course of her long and friendly association with these men, which facts and which letters and conversations to report, but she has a biographer's skill in choosing what is relevant, and the reader is confidently aware that the picture is true, distorted neither by compassion nor censure Prof G W Allport, professor of psychology in Harvard University, notes in an introduction how valuable he has found the book in the teaching of students Because Miss Evans has avoided imposing her own interpretations, students are stirred to ask questions, and hence to discover much about some common forms of mental sickness. "The first requirement in good teaching," as Professor Allport says, "is to excite greedy curiosity" These cases, he finds, do exactly that

University of Liverpool

At a recent examination for the diploma in tropical med and hygiene the following were successful

P B Acharya, A A Akiwumi, S H Bokhari E J M A Jafri Prakong Kecharanantana N H Khan T J Ma J I Maxwell, H Medina P A Y Narayanan, Margaret C Bridget O'Keeffe, A V Rao, J B Roy, G Singh, S

Dr J B Roy has been awarded the Milne medal in medicine, and Dr J I Maxwell the Warrington Yorke in tropical hygiene

Royal College of Physicians of London

At a comitia held on April 28, with Sir Russell Brain, president, in the chair, the following were elected to fellowship

J F LANDRETH Christchurch New Zealand, J L FRA London J H HALLIDAY, Sydney, R I MACDONALD, To F E PILKINGTON, South Brent, Devon, R L WAT London, A C STEVENSON, Belfast, H A TREBLE, Cant J C RICHARDSON Toronto, J F LOUTIT, Harwell, T E Newcastle upon Tyne, R B KERR, Vancouver, R N TATT Leeds, A C DORNHORST London, W S SUTTON Live B G PARSONS SMITH, London F H SCADDING, London, A LEIGH London, H V MORGAN Khartoum, L D W S Glasgow, D A WILLIAMS, Cardiff, C F HAWKINS Birmin R D TONKIN, London, H P WILLIAMS Coventry, A WILLIAMS Kampala, J R ELLIS London R A JONES Cambs, E K CRUICKSHANK, St. Andrew, Jamaica, G MACDONALD, London, B G MAEGRAITH, Liverpool, W KARUNARATNE, Colombo

The following were elected to the fellowship under by 39b, which provides for the election of non members "w have distinguished themselves in any branch of the sc or practice of medicine"

I DE B DALY F R.S, Cambridge, K G V NYLIN, Stock W G PENFIELD, O M, F R S, Montreal, G F STRONG Vanco

The following, having satisfied the censors' board, elected to the membership

J H Allison, M B Lond squadron leader R.A.F J B B M B Witwatersrand, G P Blanshard, M D Camb, C R Bo M B Sydney J A S Brine M.B Melb F I Caird B.M A. S Cooper M B Camb, J E Cosnett, M.D Witwater A J P Crowden, M B Lond, J A Davis M B Lond J B Do B.M Oxfd F E Dreifuss, M.B N.Z. M de L F M.B Adelaide Judith M Fitzsimons, M.B Camb Peter F M B N Z, A D Forrest M.B St And, T C Gibson M.B. C M P W Godfrey, M.B Lond, K L Granville-Gros M B Lond, Robert Hecker M.B Adelaide Anthony He M B Edin. Bernard Lennox, M D Durh. G D Lumb, M D J B McFadden, M.B Sydney, D C Morrell M B Lond, lieutenant R A F A E Mourant D M Oxfd C G H Ne M B Lond L J Pinto M D Bombay D E B Powell M.B. surgeon lieutenant, R.N V R., F L Richardson M B Birm, R Rischbieth, M B Adelaide, Daniel Rooney, M.B Belf, J A R L R C.P, P D Saville, M.D Lond, Eric Schiller, M.B S D J Sheehan, M D Lond, wing commander, R.A.F W D M B Glasg Eileen M. Spence M B Aberd V H Springett Lond, Bernard Tabatznik, M B Witwatersrand E J W Williams, M B Camb, Wickrama Wijenaike, M B Ceylon

Licences to practise were conferred upon the foll 125 candidates who have passed the final examination of conjoint board

Nazir Ahmed B G Andrews, Martine Y K Armstrong M Aylott, B J Bartley, Esther A Bence, A E Blumenfeld L Bowen T A Boxall, G E Brennan, D E Brooke B J Bro J D Broome E H Burgess, Brenda J Butcher P R Bu P H Byles H C I Bywater, D A O Cairns J J Camp, Gill Cann, Elizabeth A Capell J A Chappel Mary D Clarke, B Clayton Payne, Terry Coates J A B Crawford, E A P Cro D E Dart, H T Davies, K S Davies, D T F Deakin E Dingley Patricia A Dinkel Elaine O Donoghue Denise J Duc Sheila M. Eades P M Elwin Verna P Firth, J D W F C B Floyd B H Fookes, C B Franklin A. G Giddins, D Gooding, B G H Grant, H C Grocott Beryl M. L Hall P Hamber C N Haynes, Rita Henryk Gutt, Molly Hill, P Holt Judith C Howard, P J C Howe, J G J Howell, Elizabeth Hudson, Rosalinde Hurley, R H Huzzey, D E Hyams, Caroline Jones N L Jones N H Kemp, D A Kennard A G K Yuin B Ling Evelyn O Lock J A London, B H McCo B B MacGillivray T A R. Mahmoud Barbara L Mar Royston Mason, J S B Moyor Marion V Miles, J D M S F W Monkman W P N Moore, J G Morris, A. I M M W N Nicholls W B Obank, F A Orhewere, Dolly I Pak Giuseppe Pampiglione J G Parkes, G W. Peacock, G D Pe G B Phillips, T A Plumley G G Pollock C A Poulter, C A Procope, M J Prophet, Elisabeth J Rashid Victor Ratner, Ami Reed, G R E Roberts, J T Roberts, Bruce Robertson, D Rothman, Theodore Rowan, N E Rust, M. L Rutter, D Saunders G W Scott Joanna Sheldon B S Smith David S Barbara Y Stockhausen J M. Stratton Rhona Stringer M Swann D M. Symes, Lionel Tenby Ping Kun Teng D K Thomas T J Tiplady P J Toghill Chai Hee Tsao J O Udeozo, Roger Unwin, Molly E Wakely, Kenneth Wilde M. T C Wright

The following diplomas and those mentioned in our of April 30 (p 927) were conferred jointly with the Ro College of Surgeons

D C.H—L T Champness
D I.H—Ziauddin Khan
D P H—L H Seppelt

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[1] London Victor Gollancz 1954 Pp 297 15s

yal College of Obstetricians and Gynæcologists

The following were successful in a recent examination the diploma in obstetrics :

eramine M. Akhurst, James Alexander H C Allen Anne J derson M. J Barnard, C. T H Barrott Renuka Basu A G th, J G Blyth Beryl M Bromham, J W Brown Jane chanan, C D Campbell Margaret E Chitty, A R Chrispin nor B Clark, Priscilla A Clark Maxwell, J S Clayton Elinor M land, W M D Clements Mary Clothier W G Cooke R L ppock D C. Cornish Florence M. Cousley P H Crosskey b R. Davidson, D W Davis, D A. De Renzy Martin, G W naldson, D M. du Toit, C. E Elliott, Constance H Ellis, Lucy M s, E. W Evans, Joan M Evans J R Eve H. T Fay Helena M lly Graham Findlay Kathleen T Flanagan J McC Forrester W Galloway W F P Gammie, R. E M. Geldart, J A Gibson M. Goddard, H. R. Gompertz, J R Gough Sheila M Gough L. Graham F V Griffiths A B Guest, A T G Gunn E A ddock, H N Hardy, Adeline K H Heah, John Hefferman, M. Hodges, W S Horsnack D S Iles Katherine I Jack zabeth M. Jennings, A H John Isabel D Johnson Vivian K. es A R. Jordan Kevin Kelly A S L Kennedy Father S er Bernard Kirsch, William Lang L A Lees, C S Leithead C. Leslie E. R. Lester N H Logan Peter Los R. H Mackay S McAdam Kathleen M. McCartie, Doreen E. McConnell E. H. Maeckelberghe J M Manners, Muriel J Martin J F A alell, R Mol Morgan Eleanor Morrison, Mary J Mossman A. Naylor, Margaret A Norman Jean M North J W Parkin na E Partridge W F Paveley, J A Payne Mary Phillips R. Playfair T A Plumley J G Powell, Elizabeth M Price K. Prichard, Margaret J Purser Olga M Rampersaud, Amia R. n, A. M Reader D M. Reader E. G Rees B F Reichenfeld, salind M. Rewcastle, D I W Roberts Margaret J L Robinson S B Rogers J N Roper A D Rowlands, Hilary M Rowson, rgaret C. Russell Dorothy Sanderson T A. Sanderson, Kenneth ott, R. W Scott, Jane M Scott Brown Jean M Shields, M J ll, H R. Simpson W S Sinton, G H Smerdon R T Smith H Spurway R. M Stanford Hilary K R Steen Phyllis A vens, Audrey B Stevenson Dan Stewart James Stewart, F Stogle, Heather B Thompson John Thompson, David Tingle nemarie D Tupper Jack Walker Patricia G Wallis W W atson, J W S Webb J R. Welsh B F Whiteley, Sheila ckman, Gladys M. H Williams J R. Wood W J Wright, O C. Young

stitute of Cardiology, London

Dr. Lawson McDonald has been appointed assistant rector of the institute

Dr McDonald who is a graduate of the University of Cambridge lified from the Middlesex Hospital London, in 1942 After ding house-appointments there he served in the R.N.V.R. m 1943 to 1946 From 1946 to 1948 he held various appoint nts at the National Heart Hospital and the Institute of Cardio y. In 1948 he returned to the Middlesex Hospital as medical strar and in 1949 took the M.R.C.P Later he was appointed stant to the professor of medicine at the Middlesex Hospital, d visited Stockholm in connection with research into peripheral cular disorders He graduated M.D in 1952 He was awarded Rockefeller travelling fellowship for 1952–53 and during its tenure worked in Boston His publications include papers on peripheral cular disease ischæmic heart disease and mitral valve disease th special reference to the pulmonary circulation and to surgery the mitral valve

mmonwealth Health and Tuberculosis Conference

Mr Iain Macleod the Minister of Health will open this nference at the Royal Festival Hall London, on June 21 ther speakers will include Dr Johannes Holm (W.H.O) r P V Benjamin (India) Prof Etienne Bernard (France) r Walsh McDermott (U.S.A) Dr E Ross (Canada) r H G Trimble (U.S.A) Prof Arvid Wallgren (Sweden) r Geoffrey Marshall Dr George Day and Dr Honor Smith. urther particulars may be had from the National Association r the Prevention of Tuberculosis, Tavistock House North ondon, W.C 1

eview of Byssinosis Benefit

The Minister of Pensions and National Insurance has ked the Industrial Injuries Advisory Council to review the rovision made for byssinosis under the National Insurance Industrial Injuries) Acts. This review is being undertaken r the council by their industrial diseases subcommittee The chairman of the subcommittee is Sir Arnold Plant and e members include Prof R E. Lane F.R.C.P

Regulations made under the Industrial Injuries Acts at present rovide insurance cover against the disease for people who have een employed at some time since July 5 1948 and for at least wenty years in all, "in any occupation in any room where any rocess up to and including the carding process is performed in actories in which the spinning or manipulation of raw or waste tton is carried on." Benefit is not however, available unless the erson concerned has died from byssinosis or his disablement from e disease is assessed at not less than 50% and is likely to be ermanent These conditions were imposed because of the difficulty f distinguishing byssinosis from bronchitis and emphysema of non-occupational origin.

Persons and organisations are invited to submit written vidence to the secretary of the council 10 John Adam Street London W C.2 not later than June 6

Institute of Hospital Administrators

The annual conference of this institute will be held at Caxton Hall Westminster S W 1 from May 12 to 14 The principal subject chosen for discussion is Group Administration.

British Association of Physical Medicine

At a meeting held on April 23 the following officers were elected for 1955–56 :

President Lord Horder vice president Dr W S Tegner; hon. treasurer Dr A C. Boyle hon secretary Dr G O Storey; hon editor Dr H A Burt

The Medical Sickness Society

On April 26 a reception was held by the Medical Sickness Annuity and Life Assurance Society Ltd. to mark the opening of their new offices at 8 Cavendish Square London, W 1 The guests were received by the chairman, Mr R. McNeill Love

Royal Statistical Society

Study Circle on Medical Statistics—The annual general meeting of this circle will be held on Tuesday May 31, at 5 45 P.M. at the Westminster Medical School, Horseferry Road S W 1 Afterwards Dr P Armitage Dr John Knowelden, and Dr R F Wrighton will read short papers on Controlled Trials in Medical Research

Shortage of Dentists

The Interdepartmental committee under the chairmanship of Sir Arnold McNair, which has been set up by the Minister of Health and the Secretary of State for Scotland to ascertain the reasons for the lack of candidates for training as dentists, has held its first meeting and is ready to receive evidence Persons or organisations wishing to give evidence should in the first instance communicate in writing with the secretary of the committee, Mr T C. L. Nicole at the Ministry of Health Savile Row London, W 1

Food Hygiene Advisory Council

On May 2 Mr Heathcoat Amory the Minister of Agriculture Fisheries and Food announced that 11 members of this council are to represent the public 3 the trades, and 3 the workers in the trades. Lord Strong is to be chairman and other members include Mr S W Barnes, secretary to the governors of King's College Hospital Sir Harry Sinderson, F.R.C.P.E director for Sussex of the St John Ambulance Association, and Mrs. James Tweed, chairman of the house committee of St James's Hospital Balham.

Dr Stott Commemoration Fund

This fund has been started as a tribute to the work of Dr L B Stott who until his retirement owing to ill health last December spent 33 years as medical officer at Papworth Village Settlement. In view of his interest in children it is proposed to use the fund for prizes or grants for children at Papworth Village or school and/or a shelter in their playing field

Contributions should be sent to F E Redman secretary of the fund St Peter's Hostel Papworth Everard Cambridge

Hæmophilia Society

The annual general meeting of this society on April 24 was attended by 60 members and a number of doctors interested in hæmophilia Sir Lionel Whitby F.R.C.P was re-elected president and Dr R G Macfarlane was invited to become a vice president Reports on the work of groups in the South of Scotland Manchester Newcastle Sussex and Middlesex were received During the past year the society had sponsored the formation of similar societies in Australia France Holland, and Switzerland. Its address is 94 Southwark Bridge Road London, S E.1

Hospitals in Eire

The second of three sanatoria which the government of Eire is building was opened at Blanchardstown co Dublin by Mr T F O Higgins, the minister of health on April 22 The west regional sanatorium at Merlin Park Galway was opened in 1952 and the southern regional sanatorium will be opened next month The hospital at Blanchardstown will be known as the James Connolly Memorial Regional Sanatorium It has cost £$1^1/_4$ million, and it will accommodate 520 patients

It is laid out in seven 40 bed pulmonary blocks a 40 bed isolation and infective children's block four 30-bed non-pulmonary blocks (including orthopædic) and a three-storey hospital and treatment centre with operating theatres and X ray and physiotherapy departments with 80 beds The group of buildings on the 240-acre site also includes a nurses home for 100 nurses and houses and flats for the medical staff

International Society of Criminology

The third congress of this society will be held at Bedford College, London, from Sept 12 to 18, under the presidency of Dr Denis Carroll Further details may be had from the organising secretary, Mr H O Cox, 28, Weymouth Street, W 1

Indian Medical Services Dinner Club

The annual dinner of this club will be held at the East India and Sports Club Ltd , St James's Square, London, S W 1, on Friday, June 10, at 7 30 P M Tickets may be had from the secretary of the club, Medical Board Room, Commonwealth Relations Office, Matthew Parker Street, S W 1

Food Microbiology and Public Health

During its summer conference and annual meeting in Cambridge the Society for Applied Bacteriology will hold a symposium on this subject on July 4 and 5 This is open to non members, and further particulars may be had from Mr G Sykes, the hon secretary, Boots Pure Drug Co , Ltd , Microbiology Division, Nottingham

Kashmir Medical Congress

Arrangements are being made for a party from this country to attend a medical congress in Kashmir next November The approximate cost of £298 per person will include return air fare from London and travelling and living expenses in India Further details may be had from Dr R U Hingorani, 128, Harley Street, London, W 1

International Association of Gerontology

The fourth congress of this association will be held in It early in September, 1957

Vitamin E Congress

This international congress will be held in Venice Sept 5 to 8 at the Cini Foundation on the Island of Giorgio Maggiore Further details may be had from secretary, Prof Emilio Raverdino, Via Pietro Verri 4, Mi

National Insurance Benefits Abroad

People otherwise entitled to National Insurance retirem pensions, widows' benefits, or guardian's allowance will able to draw their benefit in any country in the world if d regulations submitted to the National Insurance Advis Committee are approved At present these benefits be paid to people resident abroad only if they are living in Commonwealth or in the Republic of Ireland

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The British Standards Institution have published a new stand (B S 2606) specifying requirements for flexible lead rubber g for X ray workers Copies of this standard may be obtained f the institution's sales branch, 2, Park Street, London, W 1, p 2*s* 6*d*

CORRIGENDUM *Hydrocortisone in Lesions of Soft Tissue*—In article by Dr Crisp and Dr Hume Kendall (March 5) the for of hydrocortisone was wrongly given The positions of the -O and - CO CH₂OH groups attached to the 17 carbon atom sh be reversed

Diary of the Week

MAY 8 TO 14

Monday, 9th

POSTGRADUATE MEDICAL SCHOOL OF LONDON Ducane Road, London W 12
4 P M Dr R I S Bayliss Infantilism and Dwarfism
ST MARY'S HOSPITAL MEDICAL SCHOOL, Paddington W 2
5 P M Prof F D Moore (Harvard) Endocrinology and Metabolism in Surgical Care (First of two lectures)
INSTITUTE OF CARDIOLOGY National Heart Hospital Westmoreland Street, W 1
9 30 A M Sir John Parkinson Diseases of the Aorta
MEDICAL SOCIETY OF LONDON, 11 Chandos Street W 1
8 45 P M Dr Macdonald Critchley Verbal Symbols in Thought (Annual oration.)
ROYAL FACULTY OF PHYSICIANS AND SURGEONS OF GLASGOW, 242 St Vincent Street, Glasgow C 2
5 P M Dr DeWitt Hendee Smith (Princeton) Ballistocardiography

Tuesday, 10th

ROYAL COLLEGE OF SURGEONS OF ENGLAND Lincoln s Inn Fields, W C 2
3 45 P M Dr H J Hoffman Innervation of Voluntary Muscle (Arnott demonstration)
UNIVERSITY COLLEGE Gower Street W C 1
5 15 P M Dr Mary Pickford Antidiuresis (Cushny lecture)
5 30 P M Prof H C Brown (Purdue University) Proposed Quantitative Treatment of Aromatic Substitution
KING'S COLLEGE, Strand W C 2
5 30 P.M Dr Harriett Ephrussi Taylor (Paris) Induced Transformations of Bacteria (First of three lectures)
ROYAL SOCIETY OF MEDICINE 1 Wimpole Street, W 1
5 30 P M *Experimental Medicine and Therapeutics* Dr Harry Harris Dr J Anderson Dr M D Milne Dr E M. Darmady Renal Tubules
8 P M *Psychiatry* Dr D Russell Davis Dr Norma Kent Mr Richard Lynn, Mr C V Jackson, Mr G Ettlinger Psychological Factors in Educational Disability
WRIGHT FLEMING INSTITUTE OF MICROBIOLOGY St Mary s Hospital Medical School
5 P.M Dr D A Long Response of the Host to Bacterial Infection
INSTITUTE OF DERMATOLOGY, St John's Hospital Lisle Street W C 2
5 30 P M Dr G C Wells Disorders in Pigmentation
UNIVERSITY OF ST ANDREWS Queen's College Dundee
2 30 P M Mr Andrew Logan Dr R M Marquis Prof D M Douglas Consideration of Aortic Stenosis and its Surgical Treatment

Wednesday, 11th

POSTGRADUATE MEDICAL SCHOOL OF LONDON
4 P M Prof. G Payling Wright General Pathology of Tuberculosis (Second of three lectures)
ST MARY S HOSPITAL MEDICAL SCHOOL
5 P.M Professor Moore Endocrinology and Metabolism in Surgical Care (Second of two lectures)
INSTITUTE OF DISEASES OF THE CHEST, Brompton, S W 3
5 P.M Dr F P Lee Lander Prognosis in Bronchiectasis.
INSTITUTE OF DERMATOLOGY
5 30 P M Dr R. W Riddell Pathogenesis of Fungous Infections of the Skin.
NATIONAL INSTITUTE FOR MEDICAL RESEARCH Mill Hill N W 7
5 P.M Prof E L Smith (Utah) Chemistry of Antibodies and Gamma Globulins

Thursday, 12th

ROYAL COLLEGE OF SURGEONS OF ENGLAND
5 P M Mr R V Cooke Advanced Carcinoma of the Col with particular reference to the Inflammatory Fact (Hunterian lecture)
POSTGRADUATE MEDICAL SCHOOL OF LONDON
4 P M Dr C L Cope Cortisone and A C T H
UNIVERSITY COLLEGE
4 45 P.M Prof F L Smith Mode of Action of Proteol Enzymes (First of three lectures)
KING'S COLLEGE
5 15 P M Prof Igino Spadolini (Florence) Effects of the Acet choline-cholinesterase System on the Heart. (Hallibur lecture)
ROYAL SOCIETY OF MEDICINE
5 P M *Ophthalmology* Prof J H Dunnington Hyp after Cataract Extraction
INSTITUTE OF DERMATOLOGY
5 30 P M Dr J O Oliver Antibiotics
ROYAL SOCIETY Burlington House W 1
4 30 P M Dr F B Chain F R.S Recent Advances in Ca hydrate Metabolism
ALFRED ADLER MEDICAL SOCIETY
8 P.M (11 Chandos Street, W 1) Dr W P Berring Fugue States
NUFFIELD ORTHOPÆDIC CENTRE Wingfield Morris Ortho Hospital Oxford
8 30 P M Dr A B Kinnier Wilson New Approach to piratory Poliomyelitis
HONYMAN GILLESPIE LECTURES
5 P M (University New Buildings Teviot Place Edinburg Mr G H Macnab Maldescent of the Testicle
UNIVERSITY OF ST ANDREWS Medical School Small's Wynd Du
5 P M Dr H Payling Wright Thrombosis and some less re nised Aspects of Anticoagulant Therapy
UNIVERSITY OF DUBLIN Trinity College
4 30 P M Prof G R. Cameron F R.S New Fields in Pathology (John Mallet Purser lecture)

Friday, 13th

POSTGRADUATE MEDICAL SCHOOL OF LONDON
2 P M Dr J H Middlemiss Radiology of the Acute Abdom
UNIVERSITY COLLEGE
5 15 P.M Dr L E Baylies Process of Secretion (Cus lecture)
ST MARY S HOSPITAL MEDICAL SCHOOL
5 P M Sir Heneage Ogilvie Shock
INSTITUTE OF LARYNGOLOGY AND OTOLOGY 330, Gray's Inn Road W C 1
3 30 P M Mr A R Dingley Tonsillectomy in Children Adults
UNIVERSITY OF ST ANDREWS Queen's College, Dundee
2 30 P M Prof. E J Wayne Dr Cecil Pickard Angiocardgraphy in Congenital Heart-disease

Saturday, 14th

BIOCHEMICAL SOCIETY
11 A M (University of Reading) Scientific papers

Births, Marriages, and Deaths

BIRTHS

LUNTZ —On April 25 at Sorrento Maternity Hospital, Birmingha to Pamela wife of George Richard William Neal Lu M.R C P —a daughter (Verity Anne)

WESTLAKE —On April 25 to Nora wife of Dr E Keith Westlak M D , M R C.P —a sister for Carol Anne (Diana Elizabeth).

ORBITAL LEUCOTOMY

A REVIEW OF 52 CASES

GEOFFREY C KNIGHT
M.B Lond F R C.S
URGEON IN CHARGE, SOUTH EAST METROPOLITAN REGIONAL
EUROSURGICAL CENTRE; NEUROLOGICAL SURGEON POST
GRADUATE MEDICAL SCHOOL OF LONDON

R F TREDGOLD
M.A M.D Camb D.P.M
GIONAL PSYCHIATRIST SOUTH EAST METROPOLITAN REGIONAL
SPITAL BOARD; PHYSICIAN DEPARTMENT OF PSYCHO
GICAL MEDICINE UNIVERSITY COLLEGE HOSPITAL, LONDON

om the South East Metropolitan Regional Neurosurgical Centre

In the latter part of 1949 working with Dr Ström sen at the Runwell Hospital, one of us (G C K) was le to introduce to this country the operation of orbital dercutting devised by Scoville in 1948 In 10 patients o had not benefited from leucotomy the operation ve results which in Dr Ström Olsen s opinion, justified extension to cases of neurotic tension in which Scoville d claimed success

During 1950 orbital leucotomy was used in association th Dr Ström Olsen and Dr Bierer and since 1951 ore than 50 such cases have been operated on at the uth East Metropolitan Regional Neurosurgical Centre the Brook Hospital Blackheath Elsewhere other difications of the original leucotomy have been per med, and Sargant (1953) has drawn attention to their ue He recommended their use in "intractable ychosomatic states in anxiety hysteria and in anxiety d depressive states in obsessional personalities " and pointed out that other forms of treatment notably chotherapy might succeed after operation though y had failed before.

The results obtained by our modified orbital operation peared so encouraging as to warrant a closer analysis the patients psychological condition and we have refore collaborated in this interim report The only vious English survey of orbital leucotomy is that of and Lewin (1953) of 20 cases operated on chiefly the late Sir Hugh Cairns at Oxford

Our review covers a consecutive series of 59 patients rred by various psychiatrists, usually because they such anxiety or depression that life was a misery being asked by letter to attend for follow up 4 did not ly and remain untraced 3 others had undergone cotomy previously and were therefore excluded from survey Of the remaining 52 40 were British and Polish and all save 4 had been ill for more than two rs—several of them for more than ten years

Basis of Surgical Treatment of Mental Disorder

(G C K)

The surgical treatment of mental disorder began with e injection of alcohol into the frontal lobes and has dually developed into localised anatomico physio ical investigation yielding fresh information about the chanisms of emotion and the intellectual activities the frontal regions. Our knowledge of these matters mains imperfect and the investigation continues.

The effects of the full standard leucotomy dividing central core of white matter within the frontal lobe wed that it was preferable to limit a leucotomy incision the lower segment particularly to the lower and ier fibres within the frontal lobe so as to maintain the cessary reduction in emotional tone while minimising associated intellectual deficit

Precise electrocoagulation of the dorsomedial nucleus the thalamus (Spiegel and Wycis 1949) has shown that all the effects of leucotomy may be produced by a lesion strictly localised to one area of the brain from which the afferent connections proceed to the frontal cortex

Our knowledge has been increased by experiments on individual projection pathways either by excision of limited cortical areas (cingulate superior convexity and orbital) by topectomy, and by undercutting similar areas leaving the cortex intact but severing the afferent and efferent fibres passing to and from the selected zones All these methods are intended to modify emotional behaviour while minimising concomitant damage to personality and intellect

Many of these later modifications of technique were developed because of our appreciation of the importance *of the thalamocortical connections.* Le Gros Clark and Boggon (1933) and Le Gros Clark (1948) have shown that a large part of the frontal cortex is an afferent projection area for the dorsomedial nucleus of the thalamus, comparable with the projection areas of the visual and auditory areas of the cortex, there being a well-defined point to point projection of fibres in which the anteroposterior axis of the dorsomedial nucleus projects in serial order on to the anteroposterior axis of the frontal lobe, to the cingulate superior convexity and orbital surfaces Since the dorsomedial nucleus of the thalamus is essentially a relay station for the transmission of impulses originating in the hypothalamus, the frontal cortex seems to act in part at least as the projection area for fibres concerned with hypothalamic activity and of obvious importance in emotional integration The later developments of surgical technique have concentrated on interrupting certain of these connections alone while leaving the remainder of the frontal cortex undisturbed

Preceding accompanying and giving impetus to these surgical assaults there has been a gradual change in our conception of the nature of intellectual and emotional activity No longer is intellectual function regarded as purely cognitive dependent upon the perfect function of the cerebral cortex working in isolation, and independent of any influence ascending from the basal areas of the hippocampus and hypothalamus, which are concerned in autonomic and emotional activity in the affective sphere It has come to be realised that the function of the cortex may be profoundly disturbed by stimuli ascending from the basal areas of the brain

> Dana (1921) and Cannon (1927) suggested that emotion resulted from the action and reaction of the diencephalon and the cerebral cortex the diencephalon, having received sensory impulses associated with emotion would discharge upwards to the cerebral cortex impulses which gave rise to emotional experience or subjective feeling at the same time as it would discharge downwards the motor impulses which produced emotional behaviour
>
> Nathan (1931) held that emotion and personality were localised in the region of the third ventricle and traced the development of this theory from the work of earlier observers.
>
> Alford (1933) thought that emotion and consciousness were particularly disturbed by basal lesions in the left cerebral hemisphere

Papez (1937) pointed to the ensemble formed by the hypothalamus gyrus cinguli, hippocampus and their various connections, and regarded these as the probable anatomical substratum of the emotions. In elaborating this theory he displayed the wide connections that exist between the thalamus hippocampus and hypothalamus and between the thalamus gyrus cinguli, and frontal cortex In discussing the hippocampus he pointed to the absence of evidence of olfactory function in this area, and drew attention to the facts that in rabies the Negri bodies are most abundant in the large ganglion cells of the hippocampus, and the patient shows intense emotion and hyperæsthesia to all forms of stimuli with the result that all stimuli provoke fear sometimes mingled with rage

In Papez's view somatic (including visceral) impulses entering the circuits of these basal areas may obtain emotional colour and finally reach the cortical level as "a stream of feeling" modifying the function of the cortical regions This theory suggests that the pathways connecting the thalamus to the orbital cortex and other regions of the frontal lobe contain the afferent projection systems for emotion, and it is noteworthy that each of the cortical areas receiving such pathways gives rise to efferent fibres passing towards the hypothalamus which could constitute the pathways for emotional reaction As Le Gros Clark (1952) has stated

> "It has come to be realised that intellectual and emotional processes are so intimately interlocked in any form of mental activity that *it is not possible to separate them even as* arbitrary categories Intellectual processes are only capable of normal expression if they are activated and directed by the driving power of emotional processes, The cerebral cortex *may be structurally intact but its function can be grossly* deranged if it is thrown out of gear with those more primitive parts of the brain which provide neural bases of emotional reaction"

In extending the surgical treatment of mental disorder to the sphere of the neurotic and psychoneurotic it is to the relief of an abnormal emotional charge disturbing the function of intelligence that the treatment appears to be most directly applied We seek a method which will produce the greatest modification of emotional tension without associated injury to intellectual pathways

Scoville (1949) has described the techniques for undercutting each of the three cortical areas—cingulate, superior convexity, and orbital—to which fibres radiate from the thalamus That the orbital technique is the most likely to lower neurotic tension without causing a serious intellectual deficit is suggested by the observations of Rylander (1939) which indicate that lesions of either the orbital or the inferior aspect of the frontal lobes produce changes in emotional tone rather than in intellectual or psychomotor activity Rylander (1952) in particular has shown by psychometric studies that lesions on the superolateral aspect of the frontal lobe are more likely to produce intellectual disturbances Experimental evidence also shows that stimulation of the orbital areas produces autonomic responses, and ablation of those areas tranquillity or loss of fear

Scoville's techniques were fully described and illustrated at the International Congress of Psychosurgery held at Lisbon in 1948, and subsequently published (Scoville 1949) Scoville states that he aims to undercut the entire orbital surface, including the prechiasmatic area, *isolating the entire cortex* over the orbital plate as far back as the level of the anterior clinoid process on the inner side, and as far laterally as the junction of grey and white matter on the lateral aspects of the lobe We have deliberately modified this method, omitting the lateral portion of the cut and confining the incision to a narrow arc about 2 5 cm wide passing back on the inner aspect of the lobe to a point directly beneath the anter horn of the ventricle at a depth of 5 5–6 0 cm from t frontal pole (fig 1) This modification was introdu to produce further evidence of the importance of t ventromesial fibres within the frontal lobe and to av damage to the hippocampal relays in the lateral portio of the lobe

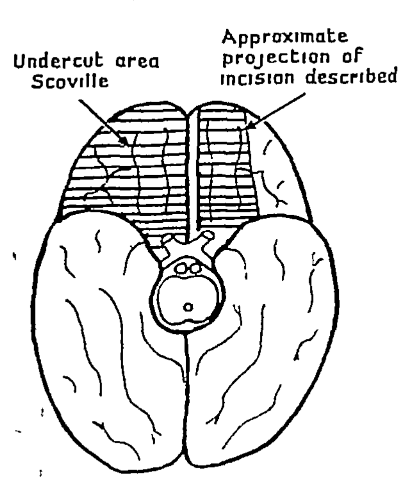
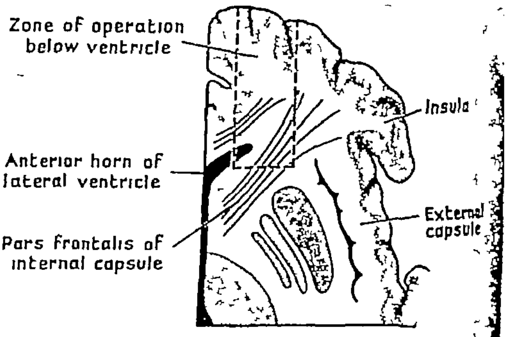


Fig 1—Approximate site and extent of incision in Scoville's (1949) undercutting operation and com[illegible] those of incision used in present

Electrocoagulation within the dorsomedial nucleu the thalamus (Spiegel et al 1947) produced benefic effects chiefly in the emotional sphere These res are by no means solely *attributable to the connect* between the dorsomedial nucleus and the frontal p jection areas (probably hypothalamic connections involved as well), but they do indicate that any signific fibres concerned in emotion and passing to the orb cortex must arise from the inner and lower area of lobe and hence could be divided close to their origin that point

Le Gros Clark (1948), discussing the afferent pathw from the thalamus, states that projection is well def between certain groups of cells in the dorsomedial nucl *and the frontal cortex, fibres proceeding to cortical* ar 8–12 approximately in order from the caudolateral part of th *dorsomedial nucleus to the anteromedial part of the* cort

Meyer et al (1947) concluded that it is the pars ma cellularis *of the nucleus that projects on* to areas 11 and in the orbital frontal cortex All the fibres projected to th orbital cortex spread thereto from the posteromedial asp of the lobe, and it is this area that has to be cut at the *of concentration* of the fibres below the pars frontalis of internal capsule rather than the outlying parts of the matter towards the inferior frontal convolution (fig 2)



Zone of operation below ventricle
Insula
Anterior horn of lateral ventricle
External capsule
Pars frontalis of internal capsule

Fig 2—Transverse section through right frontal lobe seen from ***Interrupted line shows zone of operation lying at deeper le ventricle.***

Lesions in the lateral aspect of the inferior surface of *frontal* lobes may interrupt fibres passing to the tem pole and hippocampus Efferent association tracts arise area 47 of the frontal lobe (area orbitalis agranularis) running as the uncinate fasciculus, pass lateral to the ext capsule and radiate to area 38 in the pole of the temp lobe Degeneration has been observed near to or in this fasc by Meyer et al (1947) in post-leucotomy specimens T fibres form part of a hippocampal circuit involving hip campus, fornix, hypothalamus, thalamus, *orbital* co uncinate fasciculus, temporal pole, temporo ammonic tr hippocampus, less well recognised than the well known cir hippocampus, fornix, mamillary body, thalamus, gyrus ci hippocampus Positive evidence on the function of th circuits is lacking

It has been suggested that neuronal activity could maintained in a steady state between these circuits e long periods, forming a reservoir or background for emoti expression Certainly bilateral disturbance of *these* cir seems to be undesirable

Klüver and Bucy (1939) reported changes in emoti behaviour in monkeys after excision of the temporal lo Hypersexuality has been observed after *bilateral* div these circuits Serious results have followed ablation of posterior orbital *regions in* monkeys (Ward and McCu 1947) with loss of social conscience

Hence, although it has been suggested that tion of the uncinate fasciculus is more importan refrontal leu otomy than sec on of the thalmocortical fibres, xcept where the im is relief of sceral pain, we emained unconvinced of the dvisability of this ep and decided eliberately to void these lateral nd posterior pects of the lobe nd so to avoid he possibility of ntroducing undeirable character hanges which ave sometimes en observed in e case of penetrating wounds in at area of the rain

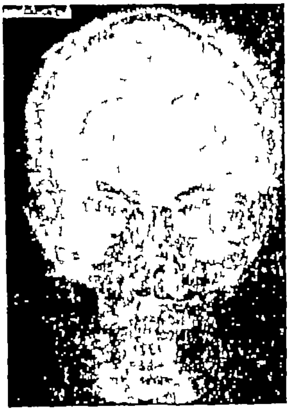


Fig 3—Position of trephine circles for orbital leucotomy

Operation

(G C K)

A transverse scalp incision concealed within the hair e is used the anterior flap being reflected forwards to pose the frontal bones as far down as the level of e orbital margins. A flap of pericranium corresponding to the exposed area is similarly reflected for ards after mobilisation of the fascia from the line of the mporal crest on each side thus exposing the frontal nes Bilateral trephined circles 3 75 cm in diameter e now fashioned at a point above the level of the frontal nuses and extending to within 1 cm of the midline on ch side (fig 3) The bone-dust thus formed is collected r later use The exposed dura is incised transversely the lower third of the exposed area (fig 4) and stay tures are inserted The frontal pole is raised from the or of the anterior fossa to determine the level of the terior clinoid process and a transverse incision 2 5 cm. le is made in the cortex hæmostasis is secured and e incision is deepened to the white matter Spatula rceps are inserted into the cortical incision and the hite matter is gradually divided with a fine suction be at the junction of grey and white matter above the bital plate on each side the incision being kept parallel the orbital roof as far back as the level of the tip of e ventricle the spatula blades being used as retractors. ould the tip of the ventricle appear in the line of the cision it is raised with the upper blade of the spatula, nd the incision is deepened to a total depth of 5 5–6 0 m beneath the ventricular tip at which level it is idened transversely to 3 0–3 5 cm The incision is actically bloodless, but occasionally bleeding points are seen towards the inner aspect of the incision near the grey matter the bleeding is easily arrested by pressure or by electrocoagulation The dura is now closed with silk sutures and the bone discs are replaced and moulded into position with a paste made from the bone dust The pericranium is brought back into position over the bone discs to conceal any minor surface irregularity, and the wound is sutured in layers

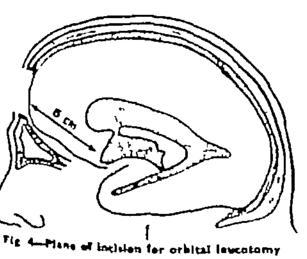


Fig 4—Plane of incision for orbital leucotomy

The postoperative course is smoother than that of a patient who has undergone major leucotomy Incontinence is hardly ever observed There is always a period of drowsiness for the first twenty four hours, and occasionally confusion for the first two or three days, but most patients are fully oriented on the day following operation Within four or five days they can be allowed out of bed, by which time the relief of tension is already apparent The mortality of this operation is obviously low so far more than 75 consecutive operations have been performed without any death

Psychiatric Survey

(R F T)

The survey included: (1) cases seen by me only after operation, and (2) cases seen before and after operation

1 Previous records were studied in detail and compared with the patients present state Since usually no formal or comparable assessment had been made by the psychiatrist who originally referred them it was not easy to be sure that comparisons were reliable; but, to get as much uniformity as possible the tables of symptoms prepared (see below) were sent back to all these psychiatrists for their comments. In most cases, but not all the psychiatrists had seen their own patients again after operation.

2 These patients were seen immediately before the operation, soon after it and some weeks after it The changes were naturally easier to assess but here also the psychiatrists who had originally referred the patients were asked to comment on the opinions formed Among these patients were 12 Poles who were reviewed in the same way by Dr G Bram of Mabledon Park Owing to language difficulties it was impossible for me to make any adequate assessment in these cases but the criteria had been agreed with Dr Bram

TABLE I—EFFECT OF OPERATION ON SYMPTOMS

Symptom	No of patients with symptoms before operation	Results after operation			
		Much better	Better	Unchanged	Worse
Depression	3[illegible]	[illegible]	8	2	
Anxiety	37	19	11	3	1
Severe insomnia	8	4	4		
Headache	8	[illegible]	5	1	
"Blackouts"	2	2			
Gross lack of confidence	1[illegible]	[illegible]	8		
Lack of interest	18	8	9	1	
Obsessions	13	5	[illegible]	[illegible]	
Phobias	4	2	1	1	
Impaired memory	7	[illegible]			5
Impaired concentration	8	1	4		3
Loss of weight	7	7			
Ideas of reference	6	[illegible]	1	3	

The general results were classified as follows:

A	Markedly improved	23	
B	Some improvement	21	(of whom some are apparently still improving)
C	Unchanged	7	(of whom 3 had shown temporary improvement)
D	Somewhat worse	0	
E	Markedly worse	1	

The various symptoms recorded before operation are listed in table I together with the change after the operation

Besides these symptoms certain others were recorded before operation: rosacea (1), cleared menorrhagia (1) improved; frigidity (3) improved in 2, but persisted in 1 hysteria (3) persisted; palpitations (2) persisted and pruritus (2) cleared up

Table I shows that a great improvement was obtained as regards depression, anxiety and loss of weight many patients' interest in their surroundings was restored, and their confidence re established, and, although most of the patients expressed themselves as having some way to go yet, they had also some confidence that they would go this way The effects on failure of *concentration* and of memory were less good, and these symptoms were in several cases made worse This does not refer to the immediate postoperative period of a week or two, when some impairment of concentration and memory was expected (but passed), *but to several months later* Nevertheless these symptoms did not appear to cause any great anxiety in the patient No deterioration in personality was evident to me or to any referring psychiatrist in any of those in category A, B, or C

RELATION OF PROGNOSIS TO VARIOUS FACTORS

Previous Personality —Table II shows the cases grouped into various personality types and separated according to their grade of improvement The only conclusion which it seems legitimate to draw here is that hysterical personalities, like hysterical symptoms, offer less ground for hope

TABLE II—RELATION OF PERSONALITY TO PROGRESS

Type	No of cases	Category			
		A	B	C	E
Dependent	14	8	5	1	0
Cycloid	4	4	0	0	0
Obsessional	11	2	6	3	0
Hysterical	5	1	2	2	0
Schizoid	13	6	5	1	1
Psychopathic personality	1	0	1	0	0
Not psychopathic	4	2	2	0	0

Ætiology and Diagnosis —The nature and severity of *the psychological factors which had precipitated the* illness were investigated but the onset was so long ago that the history given cannot be very reliable In most cases, however, some emotional stress had either caused or precipitated a breakdown Classification being a matter on which psychiatrists notoriously disagree, the symptoms listed in table II and the diagnoses listed in table III may be regarded here with some reserve The 52 cases had, however, been labelled, under the existing nomenclature, and these have been tabulated against their progress *It was clear that many* cases showed a combination of anxiety with depression, or with obsessional features as table I shows

TABLE III—*RELATION OF DIAGNOSIS TO PROGRESS*

Diagnosis	Category			
	A	B	C	E
Reactive depression	5	5		
Endogenous depression	2			
Anxiety state	8	2	1	
Obsessional state	2	6	3	
Hysteria	1	2	2	
Schizophrenic state	5	5	1	1
Psychopathic personality		1		

Previous Treatment —These patients had mostly been selected, as noted above, because they had not responded permanently to treatment, but some had previously made temporary progress under electroconvulsion therapy (E C T), and it may be of interest to record the relationship here (table IV), for it is sometimes held *that temporary* relief from E C T is an indication for operation It seems fair to conclude that the response to E C T gives no indication of what the response to orbital leucotomy is likely to be

Length of History —So far as the records could be obtained, the grades of recovery were grouped against the d of the illness (table V) Of the category C patients 2 were hysterics, this is at least as likely a rea as the length of history for their lack of improvem Though it appears that marked improvement is m likely in *shorter cases*, *some improvement* may expected from even the longest

TABLE IV—RELATION OF PREVIOUS E C T TO PROGRESS

—	Category			
	A	B	C	E
Previous benefit from E C T	8	7	1	1
No previous benefit from E C T	8	9	3	
Not previously treated with E C T	7	5	3	

Age —The correlation between age and progre given in table VI and does not seem to be significant

NEED FOR SUBSEQUENT PSYCHOTHERAPY

Some of the patients improved so much as to need further treatment, others, notably in categories B a C, made less or temporary improvement and appeared benefit from psychotherapy where it was available. was notable, however, that *some patients relapsed* wh treatment was lacking (for reasons which reflected discredit on anyone), and this point should always considered by the psychiatrist when the patients retu to his care after discharge from hospital.

MAINTENANCE OF IMPROVEMENT

The patients were necessarily seen at different peri after their operation, and observations made on th rate of progress and its maintenance, or of relapse, can readily be analysed The following facts may, how be of interest

TABLE V—RELATION OF DURATION OF ILLNESS TO PROG

Duration (years)	Category			
	A	B	C	E
Up to 5	15	7	2	1
5–10	7	6	1	0
More than 10	1	8	4	0

(1) *Some improvement was recorded in most* pat within three days after the operation, but 1 patient did *improve until seven months afterwards*

(2) This improvement went on steadily for several we in most patients, and for months in some

(3) Several patients benefited from postoperative psy therapy whereas previously they had been inaccessible

(4) Nearly all those seen more than a year after operation had remained well since the end of that *year*

(5) Several patients graded as C (unchanged) had impro but subsequently relapsed

Illustrative Cases

Case 1 —(Reported by Dr JOSHUA BIERER)

A woman, aged 42, when first seen in 1950, complained depression, inability to travel, constant fatigue, dyspe palpitations on effort, pains in various parts of the bo gastric disturbances, loss of appetite and weight, constipat insomnia, suicidal thoughts, and anxiety about illnesses as tuberculosis and insanity She seemed to be under gr emotional strain She answered questions readily b appeared to have difficulty over her memory and concen

TABLE VI—RELATION OF AGE TO PROGRESS

Age (years)	Category			
	A	B	C	E
20–30	5	3		
30–40	3	7	3	
40–50	4	5	2	1
50–60	8	4		
Over 60	3	2	2	

ion. There were however no signs of hallucination, elusions, or feelings of unreality or depersonalisation

Past History.—She had nearly died of pneumonia at the e of 9 and had had a duodenal ulcer while still at school. er appendix was removed at 20

Family History.—Her father died at 55 of cerebral hæmor age, when the patient was aged 17 but the mother lived til 1952 Mother was a very possessive dictatorial woman brother a year older than the patient, to whom she was eatly attached was killed in a motor accident before her arriage

Childhood.—She had always been shy timid and reserved ut quite normal apart from that. She was so shy that she ed to hide the fact that she was using the lavatory Felt eful in her first school but felt happier when she changed r school at the age of 15

Sexual History.—Menstruation started at the age of 17 xual relations with her husband caused pain and horror ding to frigidity Infrequent throughout marriage, and ost ceased after birth of second child

Clinical Assessment.—This patient looked younger than her e; her periods started late and her mother suppressed all evelopment towards independence. The patient sought to nd her independence in her married life but was too immature o take any responsibility *She expected pleasant feelings*, ection, love, and security but instead she experienced rror and insecurity her husband being financially unreliable aving been used to complete dependence and having xpected freedom from what she experienced as slavery she lt cornered. This caused such tension most of the time that en the security of nursing home specialists, and large doses f barbiturates did not bring her any relief Electroplexy nd prolonged narcosis, like any form of psychotherapy ought her only a very temporary relief Life to her her amily and her doctors became unbearable

Progress.—She postponed the operation twice because elations advised her against it in the end she agreed, and rbital leucotomy was performed in May, 1951 She was sent r six weeks convalescence; she hated the place she was nt to the food, and the company She returned to work in r home rather too soon, according to her own statement

Effects.—This emotionally and otherwise immature patient ho showed marked depressive, hysterical and hypo- ondriacal symptoms of long standing who underwent and used others unbearable suffering was completely relieved y the operation and enabled to live a normal life again his was achieved with so little personality change that it d not interfere with her life Two years after the operation he described her state as 'a wonderful feeling' She had no mplaints, except sometimes slight nervous depression. All r tension has gone she can run her house and travel any here (which she could not do before) She enjoys going to the atre though she does not get the same thrill out of it

Case 2.—(Reported by Dr G BRAM)

A woman, aged 40 was admitted to Mabledon Park Hospital n June 27 1951 with delusional ideas of persecution pression and *emotional instability*

History.—Apparently she was in good health until August 44 when she was wounded by a shell splinter in the right rietal occipital region She was unconscious for several urs. For four months after being wounded she had left ded paresis, and later she developed pain in the left shoulder d arm which did not respond to any analgesics.

Course of Illness.—On admission in 1951 she was apathetic nd depressed and expressed delusional ideas of persecution; he said that the pain in her left shoulder and arm was caused y some electric currents used against her by unknown eople Three weeks after admission she refused to eat nd had to be artificially fed She had twelve electroconvul ions with very good response She became symptom free nd the pain in the left shoulder and arm completely subsided. he remained well for five months and then relapsed displaying he same symptoms as before A further course of E C T was iven but without any improvement

Orbital leucotomy was done in October 1952

Effects.—The patient made remarkable progress and was ischarged in full remission four months later (the pain in he arm was no longer present) When she was readmitted for a few days in September 1953 for review it was found that he had fully maintained her remission She can look after rself and do part time work The pain in her left arm had ever returned.

Case 3.—(Reported by Dr M WATSON and R F T)

A woman was first seen in 1952, at the age of 55 She had had depression since June 1949 fluctuating in intensity It had improved somewhat with E C T (but this produced so much panic that it was stopped) and with œstrogens and dexamphetamine but she had always soon relapsed. She had a demanding and sick husband and a daughter with disseminated sclerosis One suicidal attempt Her depression was associated with guilt indecision and feelings of emptiness in her head some paranoid ideas; short occasional hypomanic phases with gross extravagance

Past History.—Subtotal hysterectomy at the age of 42 No menopausal symptoms Left mastectomy at 43 for carcinoma.

Family History and Childhood.—Apparently happy relationships with no relevant incidents. Husband a war pensioner now unreasonable and doing no work Five daughters.

Orbital leucotomy in March, 1952

Effects.—Much improved twenty five days after operation and steady *progress until seen eighteen months later* except for two interludes—a gross obstructive jaundice in July 1952 and a short phase of laziness and aggressiveness in December, 1952 The jaundice was completely painless and a secondary carcinoma was suspected but it cleared up in three weeks and was apparently an infective hepatitis In November 1953 she had no complaints, being cheerful and placid, but not unduly so She was quite rational, coöperative, and capable of coping with the domestic stress which still persisted She regarded the change in herself as wonderful

Conclusions

The criteria used to select these patients had not been carefully defined beforehand, but clearly most of them had severe anxiety or severe depression They had long records of illness and misery (misery which affected their families too) no previous psychotherapy had been of avail E C T had given little relief, and surgery was their last hope In these circumstances a high percentage of success would scarcely be looked for

This being so the success of the operation seems remarkable 23 out of 52 were markedly better, 21 somewhat better and only 7 unchanged Only 1 was worse in general, and though a few had greater difficulty in concentration or memory even these regarded themselves as better and happier A deterioration of personality was recorded in only 1 case

Though no sweeping conclusions can be drawn in an interim report on so small a series, these results suggest that orbital leucotomy should be seriously considered in long-standing severe anxiety states and depressions which do not respond to psychotherapy

It is not yet possible to say which patients will benefit most. Previous response to E C T offers no guide to prognosis nor does age The results seem more hopeful if the duration has been less, as might be expected Cases with hysterical symptoms do not seem to be suitable for the operation

All cases should be reviewed by their original psychiatrist after the operation Some patients need further psychotherapy and will benefit from it even if they did not before

We are much indebted to our neurosurgical colleague Mr G Northcroft for preparing the accompanying diagrams We would like to express our gratitude to all the psychiatrists in this region who recommended patients, supplied information and checked the assessment made later; and in particular we wish to thank Dr Bierer and Dr Bram for more detailed assessment and for permission to publish in detail the findings in cases 1 and 2

REFERENCES

Alford L B (1933) *Amer J Psychiat* 12, 789
Cannon, W B (1927) *Amer J Psychol* 39 10
Clark, W E Le G (1948) *Lancet*, i 353
— (1953) Prospects in Psychiatric Research (Proceedings of Oxford conference of Mental Health Research Fund) p. 5
— Boggon R. H (1933) *Brain* 56, 83.
Dana, C L (1921) *Arch Neurol Psychiat., Chicago* 6 631
Klüver H Bucy P C (1939) *Ibid* 42 979

References continued overleaf

UNDERCUTTING OF ORBITAL CORTEX IN CHRONIC NEUROTIC AND PSYCHOTIC TENSION STATES

R Strom-Olsen
M D Wales, B Sc, D P M
PHYSICIAN SUPERINTENDENT

D W C Northfield
M S Lond, F R C S
NEUROSURGEON

RUNWELL HOSPITAL, WICKFORD, ESSEX

The risk of personality defects has deterred many from applying leucotomy in chronic neurotic and other tension states (Strom-Olsen 1946) The patient with a well-preserved personality is likely to show greater loss than one with a simple and shallow personality (Ström-Olsen and Tow 1949), and, though standard leucotomy can be justified for a chronic disturbed psychotic who usually shows much deterioration, it is in our opinion inadvisable for the person with an intractable neurosis A different operation was therefore required for cases of chronic anxiety, obsessional neurosis, and hypochondriasis, and for some cases of paranoid psychosis and chronic depression which do not respond to electroconvulsion therapy (E C T) or other treatment

TABLE I—CATEGORY A

Case no	Diagnosis	Duration of illness before operation (yr)	Length of follow up after operation	Result
1	Chronic anxiety state	5	4 yr	Recovered
2	Chronic hypochondriasis	15	3¼ yr	Recovered
3	Chronic anxiety state	8	2¾ yr	Improved
4	Chronic hypochondriasis	11	2¾ yr	Improved
5	Psychopathic personality and drug addiction	8	2½ yr	Improved
6	Paranoid schizophrenia	5	2 yr	Recovered
7	Chronic hypochondriasis	20	2 yr	Improved
8	Chronic anxiety state	4	2 yr	Recovered
9	Chronic endogenous depression	3½	1¾ yr	Recovered
10	Paraphrenia	5	1¾ yr	Improved
11	Chronic anxiety state and depersonalisation	3½	1 yr	Recovered
12	Chronic melancholia	10	5½ mos	Not improved, died
13	Chronic depression	3	5 mos	Recovered

The method of selective cortical undercutting devised by Scoville (1949) was adopted at Runwell Hospital in January, 1950 Mr Geoffrey Knight, then neurosurgeon to the hospital, was the first to perform the operation in this country, and he operated on the first 9 cases, which are not included in the present series

In view of the experience of Scoville (1949) and Rylander (1951) the selective undercutting operation has been restricted to the orbital cortex We have no experience of undercutting either the cingulate area or the superior convexity of the frontal lobe

Material

The series consists of 27 patients operated on January, 1951 They fall into two categories (and II)

A. Patients with well preserved personalities who suffe from long standing tension states, depression, or other e tional distress which had completely incapacitated th Each had received other forms of treatment without perma beneficial results

B Chronic disturbed psychotics, usually schizophre who already showed considerable deterioration and in w the aim was a nursing improvement rather than a cure

Serious postoperative defects would be discerned rea in the first group, but less readily in the second

Of the 27 patients 8 were men and 19 women 3 m and 10 women in category A, and 5 men and 9 wome category B Their ages ranged from 23 to 61 years, being between 23 and 40, and 10 between 41 and 61

Operation

The operations have been carried out under gen anæsthesia and along the lines described by Sco (1949) and by Tow and Lewin (1953)

It has not been found necessary to use a trephine la than 1¼ in in diameter, and this size is much easier to mani late than a larger one The trephine is placed so as to br the edge of the opening in the skull as close as possible to th orbital roof, and about 1 cm either side of the middle line. I some cases the frontal sinus has been traversed, when th has happened, the mucosa of the sinus has been tur inwards towards the nasal duct, and the mouth of the cavit lightly packed immediately with 'Gelfoam' liberally po dered with penicillin and sulphathiazole, any separ portion of mucosa attached to the disc of bone has b entirely removed, and the overhanging lip of bone (for the detached posterior wall of the sinus) has been nib from the disc In such cases prophylactic penicillin is g for five days after the operation, and no complication followed the opening of the frontal sinus

During the closure of the wound the discs are suture place, and the crevice which surrounds the replaced dis filled with bone dust, this prevents the unsightly defor which may become apparent some months after the opera when the scar tissue contracts and reveals a circular groo the site of each trephination

Provided the trephine openings are low in the frontal the tip of the frontal pole will be exposed after incisi dura mater, and the lightest degree of retraction will e one to elevate the frontal pole so as to bring the optic n into view at the point where it enters the optic foramen, on each side to measure its depth from the anterior surfa the pole This is the depth to which the "cut" shoul

TABLE II—CATEGORY B

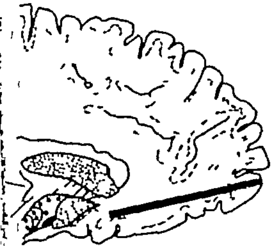
Case no	Diagnosis	Duration of illness before operation (yr)	Length of follow up after operation	Result
14	Paranoid schizophrenia	6	2¾ yr	Improved
15	Paranoid schizophrenia	7½	2¾ yr	Improved
16	Paranoid schizophrenia	9	3¾ yr	Improved
17	Chronic schizophrenia	10	2½ yr	Not improved, died of intercurrent disease
18	Paranoid schizophrenia	3½	2¾ yr	Not improved, subsequently had standard leucotomy
19	Paranoid schizophrenia	36	2¾ yr	Improved
20	Catatonic schizophrenia	17	2¾ yr	Not improved
21	Paranoid schizophrenia	4½	2½ yr	Improved
22	Hebephrenic schizophrenia	3½	2½ yr	Not improved
23	Chronic paraphrenia	8½	2¼ yr	Improved
24	Schizophrenia	7	1¾ yr	Recovered
25	Catatonic schizophrenia	6	1¾ yr	Improved slightly
26	Catatonic schizophrenia	4	1¼ yr	Unchanged
27	Paranoid schizophrenia	15	10 mos	Improved

MR. KNIGHT, DR TREDGOLD REFERENCES—*continued*

Meyer A Beck E McLardy T (1947) *Brain*, 70 18
Nathan, M (1931) *Pr méd* 39, 857
Papez J W (1937) *Arch Neurol Psychiat*, *Chicago*, 38, 725
Rylander G (1939) *Acta psychiat suppl* 20 p 3
— (1952) *Congr int Psychiat Neurol* 4 356
Sargant W (1953) *Brit med J* ii 800
Scoville, W B (1949) *J Neurosurg* 6 65
Spiegel E A Wycis H T (1949) *Proc R Soc Med* 42, 84
— — Marks, M, Lee A. J (1947) *Science*, 106 349
Tow P M. Lewin W (1953) *Lancet* ii 644
Ward, A McCulloch W S (1947) *J Neurophysiol* 10 309

le and should not be transgressed If necessary the ımal arachnoid can be broken and cerebrospinal fluid oved by suction to gain extra room. The brain is now wed to resume its normal position and a suitable site on frontal pole is chosen for the cortical incision which runs nsversely for the full diameter of the opening in the bone l approximately parallel to the roof of the orbit The cise position of the incision depends on that of veins l on the cortical pattern large veins should be avoided if sible, and an incision through the summit of a gyrus avoids ll arteries hidden in sulci The obliteration of a large vein y give rise to local congestion, making the operation more icult. The cut is now made into the brain in a plane allel to the orbital surface of the frontal lobe and about m. under it. The correct direction is repeatedly verified by oving the spatula or other instrument used for the dissec n, and reorientating oneself in relation to the roof of the it. As the cut is deepened a narrow retractor is held so as maintain the orbital surface of the brain against the orbit en the required depth has been reached (centimetre rkings on the retractor are a great help) the cut is gradually tended medially until one estimates that the middle line been nearly reached, and then laterally until increased stance indicates that the lateral cranial wall is being proached.

Hæmorrhage in the depths of the cavity is controlled by common neurosurgical methods, which are used until gentle irrigation reveals that hæmostasis is satisfactory The under surface of the frontal lobe is now re-examined to make sure that no unsuspected hæmorrhage has taken place on the outside of the brain the dura mater is approximated with silk and covered with a piece of gelfoam



1—Sagittal view of brain 1 cm. lateral to line showing usual position of lesion in rbital undercutting: IC, internal capsule; thalamus. (Tracing from myelin-stained ction.)

It is essential that anæsthesia should be induced and maintained expertly so as to avoid all cerebral congestion due to ous obstruction, cyanosis or retention of carbon dioxide he brain bulges when the dura mater is opened one should it for this to subside, checking for possible defects in the ministration of the anæsthetic in these circumstances it is er to postpone operation than to attempt undercutting

he position of the head is important; if it is moderately ended the weight of the brain causes the frontal lobe to fall ay slightly from the roofs of the orbits, thus reducing the ee of retraction necessary

Orbital undercutting is a delicate operation which nnot be performed hurriedly It demands a much gher standard of technical skill and attention to detail an does leucotomy, and should never be undertaken ithout the full panoply of neurosurgical assistance and paratus Inspection of the specimen (figs 1–3) has phasised the narrowness of the margin between the sterior part of the orbital cortex and the inferior pect of the anterior extremity of the caudate nucleus t this depth deviation from the correct plane must early be very easy and damage in either direction or at o great a depth may lead to fatal consequences.

Results

Category A.—Of the 13 patients in this category 7 ave recovered 5 have improved and 1 has shown no hange Of the 12 recovered or improved 9 have been ischarged from hospital 7 of them are living normally home and working for the first time in many years; he remaining 2 are free from symptoms and are steadily mproving but have not yet fully adapted to the stresses of life outside hospital These patients have experienced marked subjective relief of their emotional tension, distress or aggressive tendencies, according to the diagnosis Experience has shown that improvement in social adaptation may continue up to two years after discharge

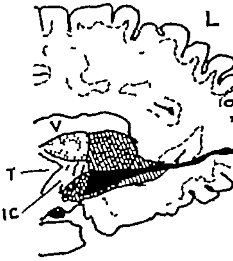


Fig. 2—Comparable (same scale) sagittal view of brain of case 12: IC internal capsule; T thalamus; V ventricle; black complete loss of tissue; hatched partial loss of tissue. (Tracing of fixed brain.)

Category B.—As was to be expected the results in this category are less favourable Only 1 has shown a social recovery but improvement has been evident in 8 of whom 4 have been discharged to their homes. This improvement has been greatest in patients who suffered distress because of hallucinations or displayed impulsive and violent behaviour However, our experience leads us to believe that undercutting of the orbital cortex is insufficient for the more severe schizophrenics because one such patient had afterwards to undergo a standard leucotomy Of the 4 chronic psychotics who were discharged 1 schizophrenic made a social recovery and has started working for the first time for many years, 2 have been relieved of their psychotic symptoms (1 is working full time and supporting her family, and the other lives a fairly normal existence and does some housework) the 4th patient, a young schizophrenic was discharged against advice and has not shown any improvement.

In both categories those patients remaining in hospital who were classified as improving have had considerable relief They are now nursed in better wards and can enjoy more freedom within the hospital

Postoperative Complications

There were no cases of clinically recognisable cerebral hæmorrhage following the operation Patient 5 in category A had epileptiform fits on the second day after the undercutting but has had none since Patients 2 and 8 in category A developed complete loss of the sense of smell, presumably through injury of the olfactory bulb tract or cortex. Patient 20 in category B had hyperpyrexia and coma for forty-eight hours but made an uneventful recovery

Incontinence of urine so distressing in many post leucotomy cases, is occasionally met with during the first

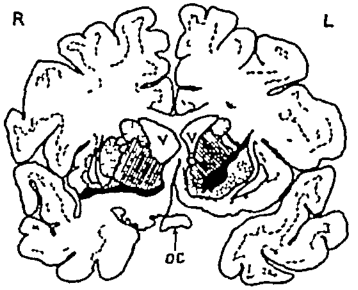


Fig 3—Coronal view of brain of case 12 at level of optic chiasma: OC optic chiasma; V ventricle; black, complete loss of tissue; hatched partial loss of tissue. (Tracing of fixed brain.)

week or two following orbital undercutting but has never persisted Except in patient 12 in category A, there were no serious or permanent postoperative complications This is in marked contrast to the standard leucotomy

Postoperative Personality Changes

The 27 patients have been thoroughly investigated for postoperative personality change, and the 24 who proved coöperative have also undergone psychometric tests by Dr Graham Foulds The 13 discharged patients have been followed up in detail at regular intervals, and not only have the relatives and the patients been interviewed, but in all cases the homes have been visited by one of our psychiatric social workers and sometimes also by one of us Special importance was attached to statements by relatives, not only on the improvement they noticed in the mental picture but also particularly on the development of undesirable symptoms In this respect the difference between the present patients and those who have undergone standard leucotomy is very striking Except patient 12, none of those in category A has shown any serious personality defect The same is true of the chronic psychotic patients, category B, though here it became less easy to distinguish between deterioration of the personality due to the psychosis and deterioration due to the operation Compared with changes seen after standard (or medial) leucotomy, there have certainly been no serious or unpleasant psychological or behavioural sequelæ There is, in our opinion, a quantitative rather than a qualitative difference There is some loss of spontaneity, which tends, however, to lessen as the months go by Some patients complain of an abnormal tiredness for the first few months Although abnormal emotional tension is eased, there is little blunting of affect—certainly never to the point of apathy For the first few weeks there is a tendency to emotional facility, with at times outbursts of laughter for little apparent reason, but this symptom has always subsided In the social sphere the recovered patients are able to work efficiently and enjoy their pleasures, contrasting vividly with post-leucotomy patients 2 of the chronic psychotic patients appeared to develop increased sexual drive However, in one of these cases there was evidence of eroticism before the undercutting It may well be that inhibition diminished

24 patients were tested psychologically four weeks after operation and 12 were tested again six to twelve months after operation The tests included Mill Hill vocabulary scale, progressive matrices, porteus mazes, thematic apperception test, Rorschach test, and Wechsler Bellevue test The outstanding features of the results so far obtained is their constancy and the absence of any sign of intellectual deterioration On the credit side are improvements in appetite, sleep, and sociability , thus patient 5 in category A, who had for years been habituated to amylobarbitone, could take little food, and was in danger of dying from starvation, quickly regained her appetite, put on weight, and could do without night sedation

Complications due to too Posterior Cut

Case 12 in category A—that of a woman of 54, with ten years' melancholia—demonstrates the danger of a lesion extending too posteriorly

After her undercutting operation in May, 1954, she was extremely drowsy for an abnormally long time She had to be fed and was incontinent She showed complete apathy, had a mask like expression, and developed signs of bilateral pyramidal damage and parkinsonism , she could not walk or stand The blood protein picture showed an absolute increase of globulin (total serum protein 6 3 g per 100 ml , albumin 2 2 g , globulin 4 1 g , albumin/globulin ratio 0 54) Within the globulin fraction the α_1 component showed a significant increase over the normal values The blood levels of urea, sodium potassium, calcium, magnesium, and chlorides were all normal, as was the CO_2 combining power The most striking feature, however, was intractable trophic ulcers both shoulders, the outer edges of both feet, the sacrum buttocks, the trochanters, the big toe joints, both heels, left external malleolus, the left fifth toe, and the left Some muscles and tendons had been eroded right thro and even the great trochanter had been eroded The ul were severely infected

In spite of intensive treatment the patient gradually deteriorated, lost weight, and eventually died, five and a h months after operation, from pneumonia, septic absc and cachexia At necropsy (Dr J A N Corsellis) the brain weighed 930 g , on both sides the surgical lesion had extended through the head of the caudate nucleus, the putamen the related segment of the internal capsule (solid black in fig 2 and 3) The area of partial damage however (as shown b hatching) appeared to be secondary and due to interference with the blood supply

In this case, it will be noted, the brain was abnormally small, and this may well explain why the section w carried too far back from the frontal pole Similar cases of severe trophic disturbances have been described following leucotomy where the cut has been made mo posteriorly than normally (McLardy 1950)

Illustrative Case-reports

Case 1 —A man, aged 34, was admitted to Runwell Hospital because of anxiety with nervous vomiting, which began during convalescence from pulmonary tuberculosis in September, 1950, and was causing physical deterioration He had alw been a nervous and sensitive person and had had bronch asthma since the age of 9 In 1946 he was discovered to ha pulmonary tuberculosis and received sanatorium treatm until October, 1949 Severe anxiety symptoms began when began to get up from a course of rest in bed. He felt afraid leaving his bed, had a sensation of "nervous tension in solar plexus," and would vomit, at first when anyth untoward happened, and then after meals regularly two three times a day He was preoccupied with the idea that tuberculosis would break out again at any time, and att of asthma, which had been rare while he was in the sanator began to recur frequently

When admitted he had already lost 21 lb Psychother and sedation failed to produce any improvement Sho after admission the tuberculosis was found to be active more, and he was treated by chemotherapy He bec increasingly anxious and vomited so much that it was im sible to continue giving him *p* aminosalicylic acid, and dietary intake was quite inadequate It was decided orbital undercutting, while his general condition rem good enough to permit the operation, was the only treat open, and the operation was performed under general an thesia in January, 1951

Progress After Operation —With continued chemother recovery from operation was uneventful After a week the patient appeared more calm, did not complain spontaneously of his fears, and took his diet well, though he denied improvement when questioned There was a gradual over all improvement in his anxiety symptoms during the following months except for two transient re-exacerbations of fear and vomiting eight and ten weeks after operation, which did not interf with the steady improvement in his pulmonary condition Eighteen months after the operation he was ambulant, longer afraid of exertion, optimistic about the future, making plans for a return to normal life He was still slightly anxious about meals, and feared a return of vomiting Unfortunately a series of upper respiratory tract infections delayed his discharge from hospital for some months, but he continued to gain confidence and was fit for discharge twenty two months after operation. There was no return of the vomiting, and he was eventually sent to a tuberculosis rehabilitation unit, where he started work as a welfare officer, driving his car about without any symptoms of fear or anxiety

Follow up —When seen nearly three years after the opera tion he had been disabled through an attack of asthma but was now well and was going back to his job He admitted that he was vastly improved and could do his work as far as his chest condition would allow him He was cheerful and there was no evidence of tension His parents stated that they could not see any detrimental traits following the operation.

Case 2 —A woman, aged 59, who had had two previous admissions to Runwell Hospital, was admitted for the th e in November 1951 The history of her neurosis went k for at least fifteen years and she was almost completely apacitated. She had depression anxiety and agitated pochondriasis She was given various forms of treatment luding E.C.T with no improvement She spent most of time in bed and, when at home could barely help with any usework, at times having to crawl about on her hands and ees.

On admission she was tense agitated and hypochondriacal th severe insomnia severe pains in the abdomen and head akness of the legs palpitations and pains in the chest e was preoccupied with her symptoms to the exclusion of ything else She swayed about, wringing her hands and oaning, continually asking for sleeping-drugs to ease her he symptoms had gradually got worse during the three or ur years before admission but were essentially the same as ough rather less severe than when she was first seen at the tpatient clinic in 1937 Bilateral undercutting of the orbital rtex was performed on Dec 24 1951

Progress After Operation.—For the first four days she was mewhat drowsy and was unaware that she had had an opera ion. Ten days afterwards she was placid and cheerful, with o agitation. She no longer spoke in a whining voice and nd-wringing was absent She could smile and laugh and id she felt much better There was no incontinence but she s rather slow in eating her food During the following two onths she steadily improved and in March, 1952 she was scharged symptom free

Follow-up —She has been visited in her home several times nce and her son also has been interviewed. When last seen ree and a quarter years after operation she was doing all her oking and housework. Whereas previously she never got up ntil 12 or 1 o clock, she was now up by 7 A.M She went out wo or three times a week and had taken up her hobbies again. he said: "There is a vast improvement in me I can now eep without drugs, I am not a bit depressed all those readful sensations are gone She read good books and had o difficulty in concentration Physically she was stronger and ad put on some weight

Case 6.—A woman, aged 38 at the time of operation had d paranoid schizophrenia for four years, during which she d been admitted three times to hospital At first her illness s characterised predominantly by apathy withdrawal and accessibility She had auditory hallucinations and delusions a persecutory nature—e g that she was always being atched by radio and television and that someone else came to the house to usurp her place whenever she went to bed went out. She believed that her husband was unfaithful her and she was frigid towards him and she lost interest in r children. She was disconnected in conversation and owed thought blockage Eighteen months before operation e began to be aggressive and attacked her husband and e nurses. She became increasingly violent and impulsive pparently in response to hallucinations. Orbital under tting was performed there was excessive bleeding at peration, and generalised epileptiform convulsions came on at evening She was incontinent for six days but after this nvalescence was smooth

Progress After Operation —A week after operation she was ill extremely apathetic but was coöperative and denied ving hallucinations. After a month she was showing more terest in her surroundings, attending occupational therapy lping with light duties on the ward and keeping herself esentable She remained coöperative and well conducted nd conversed freely There was no tension and no evidence f hallucinations nor did she voice any delusions. She went ome three months after operation and was discharged after further five weeks. At home she took up her duties in the ouse and looked after her children, and relations with her usband became satisfactory

Follow up —Seen about twenty-one months after the operaion she remained very well She was contented and there was o evidence of tension or hostility or of delusions or hallu inations; these had petered out Marital relations with er husband had become perfectly normal. She was now oing most of the housework cooking and cleaning though he did not often go shopping She had become affectionate towards her husband and children. She did not tend to lie n bed in the morning but made an early start with her housework. The husband remarked that the only thing he noticed wrong was that she could *not plan things well sometimes* showing lack of foresight but apart from that he regarded her as perfectly normal.

Case 8 —A woman aged 34 had had a chronic anxiety state with panic attacks for four years Depression and anxiety had been developing since early 1949 before which she had had a well integrated personality and held responsible executive posts She improved somewhat at first and left hospital in July 1950 only to be readmitted in April 1951, with an exacerbation of anxiety and panic attacks She was now extremely tense and trembly showing tachycardia and complaining of pains in the chest weakness of the legs and loss of energy and self-confidence In spite of sedation and psychotherapy she did not improve She had slight myxœdema following a thyroidectomy, but this was kept well under control with small doses of thyroid. For the next two years she continued in more or less the same condition. She was often lacrimose easily upset and complaining of constant fears No physical treatment improved her condition She was restless, irritable and at times excitable and she continually complained of tiredness. She underwent an orbital undercutting operation in April 1953

Progress After Operation —Immediately afterwards she was completely relaxed and at ease There was no evidence of depression and the crying bouts ceased She was amnesic for the operation She continued to make good progress and four months after the operation she was discharged and went to live with a friend who knew her very well.

Follow-up —She has been seen on numerous occasions and her social recovery has been maintained for the past two years Unfortunately she has severe purulent sinusitis which gives rise to headaches and muzziness At times she is anxious about her health but this appears to be a normal reaction Her friend is extremely pleased with the result The patient looks much better physically She can do her shopping though she cannot do her work. She still complains of tiredness and lethargy but she mixes much more socially with other people and remains quite free from neurotic symptoms.

Case 9 —A woman aged 50 began to have chronic melancholia at the menopause three and a half years before operation Her previous personality was over-conscientious and rather obsessional Five months after cessation of her periods she was admitted to the hospital under certificate after a suicidal attempt with aspirin She was depressed and expressed numerous delusions of guilt—e.g that she was contaminating all those around her and that she was the source of all the cancer tuberculosis, and blindness in the world. She had auditory hallucinations and heard people accusing her of sexual misdemeanour At this time she was experiencing menopausal vasomotor symptoms. Although she responded well to convulsion therapy she relapsed within a few months and after the third course of treatment the remission lasted only ten weeks. Recurrence of depression was accompanied by retardation; she lost all interest in life and in her relatives felt that all contact with other people was wicked and refused her food At the time of orbital undercutting she had been continually depressed for ten months

Progress After Operation —A week after operation she showed clear improvement. She was only mildly depressed showed affection for her relatives and took her diet with little persuasion Improvement continued and melancholic symptoms gradually faded out Two months later she was cheerful and active, eager to help with work on the ward and sociable and she liked to attend all the social functions in the hospital though she still occasionally expressed self accusatory delusions. She left hospital on trial and was discharged five months after operation.

Follow up —She has been seen regularly at home where she lives with her sister and as an outpatient during the year that has elapsed since her discharge and has remained quite well She shows no depression or delusions is active neat and tidy (still having a keen regard for cleanliness and orderliness) and feels capable of doing her share of household duties and shopping She likes to go out a good deal and enjoys radio and television though she finds her interest in reading somewhat diminished. Her sense of smell is absent since the operation. She looks considerably younger and smarter than before

Case 11 —A woman, aged 29 had had severe anxiety symptoms with depersonalisation for two and a half years before operation Her illness began suddenly after a minor bicycle accident in which she was not injured She was anxious and afraid to leave the house and to stay in the house by herself and she could not believe in the reality of [illegible] ment or in her own reality She could not do [illegible] and was continually preoccupied with her symptoms She was admitted to other hospitals on three occasions before her admission to Runwell Hospital and had received various courses of treatment, including E C T and insulin therapy, without relief from her symptoms Observation for nearly a year before operation showed her to be continually complaining of the symptoms and importuning for reassurance about her unreal feelings "Am I alive, or am I dead? Is it today? When will things look real?" She said she could not think of anything else or enjoy any activity There were periods of agitation when she was unable to sleep, and she took little interest in her appearance

Progress After Operation —After operation she was no longer agitated, slept without sedation, and was free from feelings of unreality, she kept herself well occupied with ward work and occupational therapy, and took full advantage of social facilities She conversed freely and easily, laughed, and enjoyed herself She was discharged six weeks after operation and at once took up her management of the home and her old interests

Follow up —She and her husband were seen separately three and a half months after discharge She had put on weight, previously having been thin and undernourished She looked considerably younger Her husband said there was a dramatic improvement There was no agitation or depression She was looking after her home very well and getting up early She no longer presented any symptoms of depersonalisation and had not once asked for reassurance She found that her housework was not quite enough and would like more to do She had normal initiative She enjoyed such entertainments as cinema, radio, and dancing, and there was no evidence of impairment of drive or concentration At times she complained of tiredness, but this in no way interfered with her activities She has now obtained employment and is working full time

Case 13 —A dock labourer, aged 31, had depression with paranoid delusions for three and a half years before the operation Previously he had enjoyed excellent health except for an accident at the age of 30, when he fell 60 feet, fracturing his spine and wrist, without persisting disability At the onset of his mental symptoms he would return from work morose and disgruntled and would sit brooding for hours Shortly after this he expressed paranoid ideas about his work-fellows, became increasingly agitated, depressed, and sleepless, and believed that men were surrounding the house, talking about him, and trying to get in at him This culminated in his admission to hospital after attempting suicide by cutting his throat

On admission he was tense, depressed, and retarded, with little spontaneous activity, and showed a tremor of his hands and lips He said that his work mates had "put the pressure" on him, had called him a "wrong 'un" and a "copper's nark." He heard a voice in his head repeating "He is insane, he is insane" and other derogatory remarks He said he had been forced to protect himself and on one occasion had attacked a work-fellow with a knife He had also been drinking heavily for some months He was full of remorse for his wrong doings and felt that he was unworthy of his family

Response to E C T was good, and he left hospital and returned to work after eight weeks, but he soon began to drink again, and later became depressed and was readmitted, having been home for six months after a second suicidal attempt Further courses of E C T produced only temporary improvement, and he remained in hospital in a depressed and deluded state Orbital undercutting was performed three years after his original admission, and at this time he had been continually depressed for a year

Progress After Operation —After operation tension was still present at times, but he was not depressed. During the two postoperative months before his return home he gradually lost his tension, and was happy and friendly with the other patients whom he had previously believed were talking about him

Follow up —Four months after operation he remained well and entirely free from psychotic symptoms, depression, and tension and appeared placid and contented He looked after himself well spontaneously, occupied himself with jobs about the house, reading, and going for walks Immediately on discharge he was eager to start work again He was advised to take it easy for a while, but there is no doubt that he is now fit to do a full day's work

Discussion

Scoville (1949), who devised the first undercutting operations as opposed to topectomies and gyrectomies, suggested three sites for the operation according to the nature of the disorder (1) the superior convexity of the frontal cortex corresponding to Brodmann's areas 9 and 10; (2) the medial frontal cortex cingulate area, and (3) the orbital cortex areas 11 and 13 Scoville regards the undercutting of the orbital cortex as the ideal operation for the relief of chronic neuroses and milder mood disturbances, because of the almost complete absence of personality changes Our best results are in just these conditions—i e, chronic anxiety states and chronic depressions—but some of the patients with a paranoid psychosis who had much tension or suspiciousness also benefited greatly from the operation On the other hand, in severe psychotics the operation may be found insufficient quantitatively As mentioned above, case 5, in category B, had subsequently to undergo a standard leucotomy

In such an unpredictable field as neuro anatomy, especially in the present state of our knowledge, a discussion on correlation between clinical findings and operative lesions, examined post mortem, is not likely to be very profitable Much more material from recorded cases will have to be examined It may be of interest, however, to note that, according to Fulton (1951), the hypothalamus projects to the cerebral cortex by way of two main groups of thalamic nuclei, the anterior and the dorsomedial nuclei As regards the dorsomedial nucleus, the most medial portion is that which receives neural messages from the hypothalamus, and this projects to the orbital surface, especially the anterior part and the frontal pole (Le Gros Clark 1948, Le Gros Clark and Meyer 1950) The lateral part of the dorsomedial nucleus sends fibres to the convexity of the frontal lobe Neurophysiologists suggest that this tract provides an essential relay mechanism through which the activities of the hypothalamus can immediately influence those of the higher functional levels of the cerebral cortex Interruption of the pathway between the magnacellular portion of the dorsomedial nucleus and the orbital cortex may diminish to a very large extent the number of impulses influencing "consciousness," and in this way, it has been argued, provide relief from a state of tension

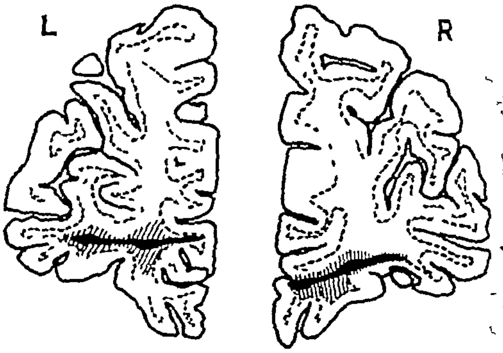
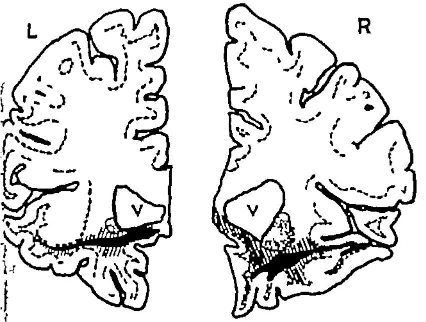


Fig 4—Coronal section 3 cm posterior to frontal pole (case 17): black, complete loss of tissue, hatched, partial loss of tissue (Traced from myelin-stained section)

In this connection the following neuro anatomical observations are of importance Patient 17, in category B, a woman of 26 with long standing paranoid schizophrenia and much deterioration, who was operated on 8 October, 1951, died of intercurrent disease (carcinoma of the ovary) two and a half years later We are indebted to Dr Corsellis for the following report

"At the frontal pole on both sides there was a horizontal slit-shaped cavity 2 0 cm × 3 0 mm, which first penetrated the polar cortex and then opened out into the white matter deep to the orbital surface On both sides, at a coronal level 3 0 cm. behind the frontal pole (fig 4), the medial two-thirds of the orbital cortex had been undercut, although on the left



g. 5—Coronal section 4 cm. posterior to frontal pole (case 17): V ventricle; black complete loss of tissue; hatched partial loss of tissue. (Tracing from myelin-stained section.)

e the lesion was slightly more dorsally placed The widest onal extent of the undercutting was at a level 4·0 cm from e pole (fig 5) when the entire width was affected Posterior this level the lesions rapidly narrowed and they died out ntral to the most anterior limits of the heads of the caudate cleus—i.e., 5·0–5·5 cm. from the frontal pole (fig 6)

Histologically the cavities were encircled by a narrow ge of demyelination always less than a few millimetres deep part from the entry wounds the frontal cortex was not preciably affected and the only other changes were condary ones related to the primary lesions. These included lateral degeneration of a small segment of the internal psule and of the medial part of the dorsomedial nucleus of e thalamus.

Although this case, from a clinical point of view is a d example because the patient was already grossly teriorated when operated on the neuro anatomical anges are of great interest because they seem to confirm at at least part of the tracts carrying visceral impulses m the hypothalamus via the thalamus had been ered The results of a more detailed investigation of e brain by Dr Corsellis will appear elsewhere No hard d fast conclusion can of course, be drawn from this gle specimen; but continued study along these lines specimens become available will further our progress wards a more definitive method of relieving mental order by operation

Summary

The results in 27 patients who have undergone bilateral dercutting of the orbital cortex are described

The patients were divided clinically into two groups: with well preserved personalities, of whom 7 were ronic neurotics (category A) and 14 who were deteriorated psychotics (category B) In category A 9 patients were afterwards discharged, of whom 7 were regarded as recovered and 2 as improved In category B 4 patients were discharged, of whom 1 was a social recovery 2 were improved and 1 was not improved

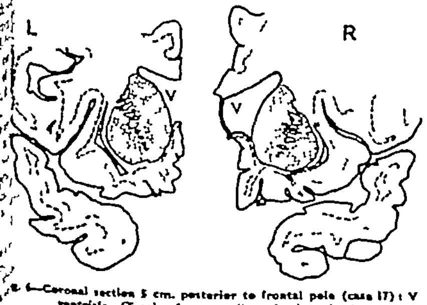
Of the remaining 3 in category A 2 improved in category B 5 did not improve and 1 of these subsequently underwent a standard leucotomy

There was no immediate postoperative death, but 1 patient with an abnormally small brain, in whom the cut had been carried too posteriorly died from extensive trophic ulceration five and a half months after operation

The postoperative personality changes have been negligible or very slight and have never reached the disturbing proportions seen after standard or medial leucotomy

The absence of serious personality defects and other complications after undercutting of the orbital cortex renders this operation preferable to standard leucotomy in chronic and apparently intractable neurosis or depression

This operation is also to be recommended in well preserved psychotics who exhibit tension and psychomotor unrest due to delusions and hallucinations



g. 6—Coronal section 5 cm. posterior to frontal pole (case 17): V ventricle. (Tracing from myelin-stained section.)

Our thanks are due to Dr J A. N Corsellis, neuropathologist to Runwell Hospital for neuropathological reports and to Dr Graham Foulds, senior psychologist to the hospital, for psychological investigations We are also greatly indebted to Dr S Wiseberg registrar at the hospital for assistance in the preparation of case histories and follow up interviews

REFERENCES

Clark W E Le G (1948) *Lancet*, i, 353
— Meyer M. (1950) *Brit med Bull* 6 341
Fulton, J F (1951) Frontal Lobotomy and Affective Behaviour London p 44
McLardy T (1950) *J Neurol Psychiat* 13 106
Rylander G Personal Communication quoted by Fulton (1951) p 124
Scoville, W B (1949) *J Neurosurg* 6, 65
Strôm Olsen R. (1946) *Proc R Soc Med* 39 431
— Tow P M. (1949) *Lancet*, i 87
Tow P M Lewin, W (1953) *Ibid* ii, 644

THRUSH ŒSOPHAGITIS WITH PHARYNGEAL INCOÖRDINATION

TREATED WITH HYDROXYSTILBAMIDINE

O H. WOLFF
M.D Camb., M.R C P
LECTURER IN PÆDIATRICS AND CHILD HEALTH UNIVERSITY OF BIRMINGHAM

B W PETTY
M B Birm., D Obst.
RESIDENT MEDICAL OFFICER, THE CHILDREN'S HOSPITAL, BIRMINGHAM

R ASTLEY
M.B Birm., D.M R
CONSULTANT RADIOLOGIST THE CHILDREN'S HOSPITAL

J M. SMELLIE
O B.E., T D M D Edin., F R.C P
PROFESSOR OF PÆDIATRICS AND CHILD HEALTH IN THE UNIVERSITY OF BIRMINGHAM

This report describes thrush œsophagitis in two new born infants in whom a disorder of swallowing led to aspiration pneumonia Treatment with hydroxystilbamidine not previously used in this condition was effective.

Case reports

Case 1—A girl aged 17 days and weighing 6 lb 6 oz (birth weight 6 lb) was admitted on July 24 1954 with a 24 hour history of vomiting and refusal of feeds.

Her general condition was fair A white membrane from which *Candida albicans* was isolated covered the tongue and buccal mucous membrane The vomiting and refusal of feeds suggested spread of the thrush to the œsophagus Treatment with gentian violet (1% paint to the mouth, and 0 01% 4 ml three times daily to swallow) was started

During the next 3 days reluctance to feed and occasional vomiting persisted, and her general condition remained unchanged Then, on July 28, she developed bronchopneumonia, confirmed by radiography Despite a course of sulphadimidine her condition deteriorated further during the next 48 hours The oral thrush persisted, and a profuse viscid discharge now poured from nose and mouth On July 30 a course of penicillin, previously avoided because of the thrush, was started, but the downhill course continued, and it seemed that the infant had not much longer to live At this stage vomiting, inability to swallow either food or the secretions from the nose and mouth, and repeated attacks of cyanosis despite oxygen therapy were the outstanding features The pulse rate was 180 and respirations were 80 per min Feeds had to be given by œsophageal tube passed through the mouth, because the nostrils were blocked by œdema and secretions Frequent sucking out of the nose, mouth, and pharynx was necessary to save the infant from suffocation On July 31 the house physician noted in the case records "I fear the worst"

On Aug 1 sulphadimidine, penicillin, gentian violet, and œsophageal feeds were discontinued, and an intravenous infusion was started At 10 P M the first dose of hydroxystilbamidine was given 15 mg (5 mg per kg body weight) dissolved in 0 75 ml of water was injected slowly into the rubber tubing above the drip chamber This dose was repeated 12-hourly Next morning she had improved remarkably, her respiration was slower (64 per min) and less laboured, and her pulse rate had fallen to 140 That night, however, she had a further attack of cyanosis This led us to start a course of streptomycin in addition to the hydroxystilbamidine, because it was impossible to decide whether there was a true thrush pneumonia or a bacterial aspiration pneumonia secondary to the thrush œsophagitis and stomatitis The latter diagnosis was supported in retrospect by the isolation of a coagulase positive *Staphylococcus aureus*, sensitive to streptomycin but insensitive to penicillin, from a blood culture taken on Aug 1

During the next week the baby improved steadily The nasal discharge and obstruction cleared within 24 hours of starting treatment with hydroxystilbamidine, the oral thrush membrane disappeared rapidly, no further *C albicans* was isolated, and radiography on Aug 6 showed decreased pulmonary involvement Because of this improvement and also because signs of thrombophlebitis had appeared, intravenous fluids and hydroxystilbamidine were stopped after a 6 day course, and oral feeds were begun again She took small amounts well, but, as the feeds were increased, she again started to cough and splutter, and on Aug 8 she had an attack of cyanosis On Aug 11 fluoroscopy showed bilateral basal collapse as well as incoördination of swallowing, which caused much iodised oil to enter the tracheobronchial tree Œsophageal feeding was recommenced and again she improved, though fluoroscopy on Aug 20 showed persistence of the incoördination

On Aug 26 feeding by teat was attempted once more, and this time there was no spluttering or choking Further progress was very satisfactory The baby was discharged on Sept 19, and when she was last seen on Nov 22 her condition was excellent, she had gained 4 lb and a chest radiograph was normal

Case 2 —A boy, aged 24 hours, was admitted on Oct 19, 1954 Pregnancy and delivery normal Birth weight 7 lb A few hours after birth a generalised petechial rash had appeared.

His condition was good, and there were no other abnormal signs A blood-count showed 56,000 platelets per c mm and 6000 leucocytes (1140 polymorphs) per c mm The discovery of thrombagglutinins (Stefanini and Dameshek 1953) and leukagglutinins (Dausset et al 1954) in the sera of the infant and of his mother explained the purpura and granulocytopenia

No fresh petechiæ appeared after admission, although the platelet-count on Oct 23 was only 32,000 per c.mm On Oct 25, however, he had purulent conjunctivitis of the right eye, omphalitis, septic blisters on the face, and oral thrush Oral and conjunctival swabs grew *C albicans* A *Staph aureus*, sensitive to aureomycin but insensitive to penicillin, was also isolated from the conjunctiva The septic skin lesions, conjunctivitis, and omphalitis cleared rapidly with a 6-day course of aureomycin 20 mg 6 hourly The thrush stomatitis was t[illegible] gentian violet paint Occasional vomiting suggested spread of the thrush to the œsophagus, so the baby was also given gentian-violet to swallow

Even after aureomycin had been discontinued on Nov 1, the thrush spread further until the tongue and oral mucosa were completely covered, and on Nov 2 *C albicans* was isolated from stomach washings A blood count on Nov 3 showed 7400 polymorphs per c.mm but still only 135,000 platelets per c mm His condition gradually deteriorated

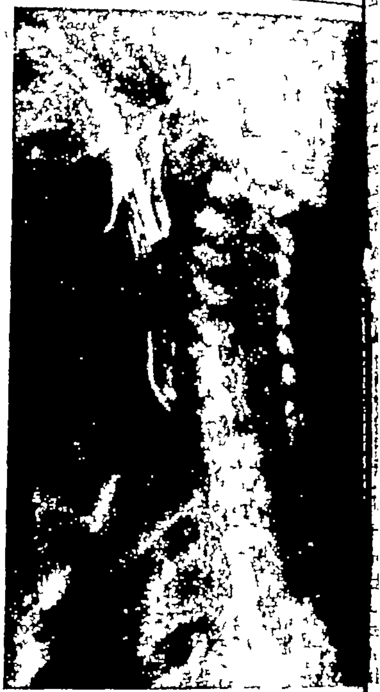


Fig 1—Case 2 Incoördinated swallowing oil has passed into nasopharynx and trach

He became reluctant to take feeds, milk was retained in mouth and dribbled from the corners, there was splutte and he had several attacks of cyanosis It was often nece to suck out his nose, mouth, and pharynx, where much st mucus accumulated and interfered with breathing

On Nov 4 one of us (R A) examined the infant flu scopically the contrast medium was held in the mouth rejected, very little was swallowed If contrast me was injected into the back of the mouth or pharynx, swallo was seen to be incoördinated Iodised oil passed up into nasal cavity and down the trachea, little entered the phagus (fig 1) If oil was injected directly into the œsoph it passed down reasonably well The picture was th pharyngeal incoördination of swallowing The lungs were

During the next 24 hours his condition deteriorated fu The temperature rose to 101 6°F, the pulse rate to 19 the respirations to 90 per min

On Nov 5 local treatment to the mouth was discont and intravenous fluids were substituted for oral feeds S taneous treatment w hydroxyst bamidine mg 12 hou was start being give the sa method as case 1 Th improveme during th next 2 da was remark able Afte hours trea ment wit hydroxyst bamidin cultures fr oral swabs a stomac washings d not grow *albicans* Th oral membr started to on Nov 7, by Nov 12 mouth

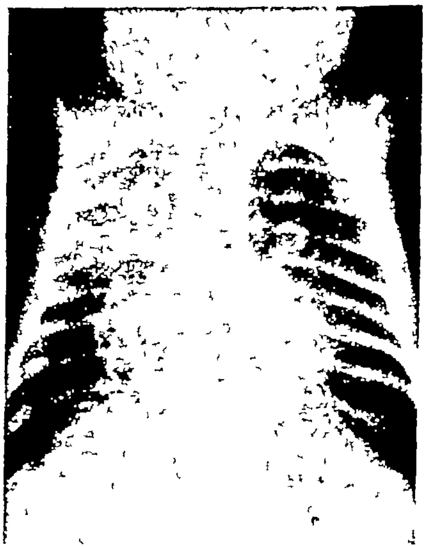


Fig 2—Case 2: aspiration pneumonia.

ered with healthy looking mucosa. Because of this rapid rovement, and also because the leg into which the intraven fluids and the drug had been given showed signs of throm hlebitis, hydroxystilbamidine was stopped on Nov 9 and feeding restarted Within 24 hours all the symptoms of ryngeal incoördination recurred with reluctance to feed spluttering Frequent suction of secretions from the mouth nostrils was necessary Oral feeding had obviously been arted too soon.

On Nov 13 the baby developed pneumonia: a radiograph wed extensive consolidation in both lungs, consistent with ration into the bronchial tree (fig 2) A blood-count wed 4500 polymorphs per c.mm and 320 000 platelets c.mm *Staph aureus* was isolated from oral and nasal retions. Treatment with streptomycin and erythromycin, which the organism was sensitive was started The infant nursed in oxygen and tube fed After an anxious few days again improved and fluoroscopy on Nov 22 showed a mal though rather slow swallowing reflex. Consequently l feeding was restarted and further progress was uneventful. radiograph on Dec 8 showed resolution of the consolidation, d he was discharged on Dec 11 When he was last seen on c. 31 his condition was excellent and he had gained 2lb ce discharge.

Discussion

cidence

Thrush infections are common during early infancy dlam and Henderson (1942) swabbed the mouths of unselected infants at intervals during the first ten ys of life they isolated *C albicans* from 11 all of om developed clinical thrush a further 3 infants, king a total of 23% developed thrush before leaving pital. Anderson et al (1944) found an incidence of 7% of clinical thrush in newborn infants and, like dlam and Henderson noted that, whenever *C albicans* s cultured thrush developed in two or three days. e use of antibiotics has made thrush infections even re frequent (Amlie 1952 Holzel 1953 Nikolowski 1953) ommonly these infections are mild remain localised the mouth or skin and respond readily to gentian let or to borax in glycerin Probably such mild cases en remain undiagnosed and recover spontaneously t infrequently however the infection takes a less lign course spreads beyond the mouth into the rynx oesophagus larynx, and bronchi or rarely into lungs or blood-stream, and may kill the infant

bbs (1938) at the Children s Hospital, Birmingham found ng a three-year period 22 instances of thrush oesophagitis cropsies on infants. He regarded the thrush as the cause eath and not as a terminal complication of some other dition. Ludlam and Henderson (1942) over a four year od found 20 cases of thrush oesophagitis at necropsy The nce in infants who died after forty eight hours of life 6·6% The thrush appeared to be the cause of death in cases. In another series, of 2 40 infants who survived for e than forty-eight hours the same observers found 163 of thrush. 20 of these died from various causes necropsy done in 18; in 8 the thrush had spread to the pharynx l in 7 of these it had also invaded the oesophagus In 2 s it had spread to the stomach Lederer and Todd (1949) nd either pharyngeal or oesophageal thrush in 7 of 28 ropsies on newborn babies and in 10 of 170 necropsies on ants 1–12 months old

Whereas the diagnosis of oral thrush is usually easy n thrush in early infancy is often unrecognised par ularly when it occurs without oral thrush The atest difficulties however arise in the diagnosis of ush involving the pharynx oesophagus, larynx or e respiratory tract below the larynx The *British dical Journal* (1950) stated that the diagnosis of tabuccal thrush is a matter of conjecture and can nerally be made with certainty only after death derer and Todd (1949) thought that the diagnostic ficulties in the living and even at necropsy might be ponsible for fatal thrush lesions remaining undetected d unrecorded In the presence of oral lesions a deteri ation in an infant s condition will suggest extension of e thrush; but pharyngeal lesions may occur in the sence of or with only inconspicuous oral thrush

Clinical Features

In view of the difficulty of exact definition of the extent of the thrush infection, we shall for convenience refer to the syndrome as "thrush oesophagitis," realising that the pharynx and respiratory tract may also be involved Ebbs (1938) Ludlam and Henderson (1942) Adams (1944) and Lederer and Todd (1949) described the clinical features of this syndrome Their descriptions agree closely with each other and with the findings in our cases

Initially there is crying during feeds and regurgitation or vomiting, which is occasionally projectile, the vomit may contain blood. Then feeds are refused or retained in the mouth and dribble from its corners, much thick mucus accumulates in the mouth and nose Despite correction of dehydration an intense toxæmia develops often with a subnormal temperature During feeds attacks of cyanosis occur which Ebbs (1938) ascribed to aspiration of vomit Lederer and Todd (1949), however postulated pharyngeal incoördination leading to direct entry of milk into the respiratory tract. This hypothesis we have been able to prove by fluoroscopy and by ciné-radiography by the technique described by Astley (1955),

In both children there was a disorder of deglutition largely restricted to the pharynx transit through the oesophagus was relatively normal and only hindered by respiratory distress. Much of the opaque medium remained in the pharynx for some seconds contrasting strongly with the normal rapid passage The pharyngeal space remained open and its communicating passages patent; the larynx did not rise and the nasal cavity was not closed off by the soft palate In consequence iodised oil passed upwards into the nose and downwards into the larynx and tracheobronchial tree During much of the time the epiglottis remained erect amidst the contrast medium There was not however an absolute paralysis; occasionally the larynx rose and the pharyngeal space was obliterated Infrequently a bolus passed much more normally and the epiglottis turned down with it in the usual manner (Ardran and Kemp 1952)

These findings suggest that the pneumonia, which has been regarded by previous writers as such a constant terminal event (Ebbs 1938 Ludlam and Henderson 1942 Glanzmann and Riniker 1950) is at least sometimes due to a complicating disorder of swallowing A true thrush pneumonia is probably rare (Adams 1944 *British Medical Journal* 1950) the causal organisms usually being secondary pyogenic invaders, particularly *Staph. aureus* (Ludlam and Henderson 1942, Adams 1944 Lederer and Todd 1949, Glanzmann and Riniker 1950, Amlie 1952)

Treatment with Hydroxystilbamidine

Hydroxystilbamidine is one of the series of aromatic diamidine compounds synthesised by Ashley and Harris (1946) in the laboratories of Messrs May & Baker Fulton (1944a) found it of prophylactic value against *Trypanosoma rhodesiense* inoculations in mice In *Leishmania donovani* infections in golden hamsters it was as effective as stilbamidine (Fulton 1944b) Hydroxystilbamidine has been used in the treatment of multiple myeloma (Snapper 1948) kala azar (Sen Gupta 1949) mucocutaneous leishmaniasis (Snapper 1952) blastomycosis (Snapper and McVay 1953 Smith 1953 Colsky 1954 Sutliff et al 1954 Weinberg et al. 1954) and a coccidioidal infection involving a single bone (Grebe 1954) Trigeminal neuropathy, which is a relatively frequent and distressing complication of stilbamidine treatment (Napier and Sen Gupta 1942 Collard and Hargreaves 1947, Schoenbach and Greenspan 1948) and led Snapper et al (1952) and Curtis et al. (1954) to abandon its use has not been reported after treatment with hydroxystilbamidine

We have not found an account of thrush infections in man treated with stilbamidine or hydroxystilbamidine A trial of these compounds was suggested by their success in other mycotic infections Solotorovsky et al (1954) showed that stilbamidine and hydroxystilbamidine are moderately active against *C albicans* in vitro but inactive in mice However, failure of a drug to cure fungus infections in mice does not necessarily imply failure in man For example, Schwarz and Adriano (1953) failed to arrest experimental blastomycosis in mice with stilbamidine, yet in human infections its value is beyond doubt Schoenbach and Greenspan (1948), in their excellent review of the aromatic diamidines, state that the host drug relationship is as important as the host parasite and parasite drug relationships Smith (1953) and Snapper and McVay (1953) expressed similar views

The pharmacology of hydroxystilbamidine has been reviewed by Snapper et al (1952) and Smith (1953) The following brief account is largely based on these reviews and that of Schoenbach and Greenspan (1948), which deals with the aromatic diamidines in general

Hydroxystilbamidine is 4 4′ diamidino 2 hydroxystilbene The compound used in our cases was 4 4′ diamidino 2-hydroxystilbene di β hydroxyethanesulphonate, which contains 54% of base For brevity we have used the term hydroxystilbamidine in place of the full chemical name of its salt After an intravenous dose of 2 mg of stilbamidine or hydroxystilbamidine per kg body weight only about 15% is excreted in the urine in twenty four hours After daily doses for seven or eight days the amount excreted in the urine increases progressively to a maximum of 70–80% in twenty-four hours, this suggests that the body proteins gradually become saturated with the diamidines, after which the excess is largely excreted in the urine It is likely that the remarkable adsorptive qualities of the diamidines account for the progressive improvement which may take place long after cessation of therapy Snapper et al (1951) found traces of diamidines in the body three years after administration

Administration —Sen Gupta (1949) and Grebe (1954) observed that hydroxystilbamidine given intramuscularly caused pain at the site of injection, Smith (1953) condemned the intramuscular route for the same reason and as a possible cause of local necrosis The intravenous route appears preferable, though Snapper and McVay (1953) noted little pain or tissue reaction after intramuscular injection with procaine (75 mg of hydroxystilbamidine in 2 ml of 5% glucose in physiological saline solution containing 20 mg of procaine) Snapper (1948) and Sen Gupta (1949) dissolved hydroxystilbamidine in 10 ml of water and 25 ml of 25% glucose respectively and injected it slowly into a vein Snapper (1952), Smith (1953), Colsky (1954), Grebe (1954), and Weinberg et al (1954) gave 225 mg daily (the dose for adults) dissolved in 200–300 ml of 5% dextrose or of saline solution by continuous intravenous drip over periods ranging from half an hour to three hours Continuous drip is probably preferable to intravenous injection, which may be followed by thrombophlebitis After rapid injection transient pallor, dizziness, a fall in blood pressure, and tachycardia have been reported (Schoenbach and Greenspan 1948, Smith 1953)

Published reports deal mainly with adults, and we have been unable to find an account of hydroxystilbamidine used in infants At this age daily intravenous injections are difficult to give In our two cases we discontinued oral feeds, administered fluids by continuous intravenous drip, and injected the hydroxystilbamidine (15 mg in 0 75 ml of water) slowly into the rubber tubing above the drip chamber The occurrence in both infants of venous spasm after injection, and later of thrombophlebitis, suggests that it might be better to give the compound by continuous drip over two or three hours

Smith (1953) noted that a precipitate forms when concentrations greater than 0 5% of stilbamidine are added to human serum, and suggested that this may explain the occasional immediate toxic effects after intravenous injection of concentrated solutions We also noticed a precipitate in the drip chamber when hydroxystilbamidine was injected into the rubber tubing while plas[illegible] being infused, though our infants showed n[illegible] toxic effects After this observation the hydroxystilbamidine was injected into glucose and saline solutions, with which no precipitate formed

Dose —The dose commonly recommended for adul 3–5 mg per kg body weight daily or on alternate da As infants usually require relatively greater amounts chemotherapeutic agents, we decided on a dose of 5 m per kg, and the infants' very poor condition led us t repeat the dose twelve hourly Treatment was contin for six and four days respectively (total doses 180 m in case 1 and 120 mg in case 2) Because of the rate of excretion of hydroxystilbamidine, the rapid appearance of the thrush lesions, and the developme thrombophlebitis we decided against a longer cours treatment The *optimum therapeutic régime* will only discovered after further *trials of hydroxystilbamidine* in severe thrush infections Our experience with the two cases has convinced us that such trials are justi whenever the response to simpler remedies is unsa factory, especially when *the infection* has spread bey the skin or the mouth

Adjuvant Therapy

As secondary pyogenic invasion is important, it advisable in the more severe cases to use a potent bacterial agent in addition to hydroxystilbamidine—in case 1, where streptomycin was given The disapp ance of the thrush membrane from the mouth must be taken as evidence that there can be a return to feeding, this mistake, which we made in both ca led to the development of pneumonia There w latent period between the disappearance of the membr and the return of normal deglutition—an observatio not recorded previously, probably because before advent of hydroxystilbamidine no such seriously infant had survived It appears advisable to fo intravenous feeding, which is necessary at the heig the illness, by a period of tube feeding We su that after the disappearance of the thrush memb fluoroscopy should be employed to demonstrate no swallowing before oral feeds are restarted

Summary

A severe thrush infection of the upper alimentary respiratory tracts may be accompanied by a cl picture due to incoordination of swallowing

This incoördination may lead to pneumonia

Hydroxystilbamidine was an *effective form of* t *ment in the two cases described*

Secondary pyogenic invasion is an important comp tion requiring additional treatment

Disordered swallowing may persist for several after the disappearance of the thrush membrane f the mouth, fluoroscopy is advisable before rec mencing oral feeding

We are indebted to Dr H S Baar for suggesting demonstrating the presence of leukagglutinins and thr *agglutinins in case 2*, and to Dr W R Thrower who first d our attention to the possible value of hydroxystilbamid thrush and helped us with case 1 We gratefully acknow the invaluable nursing services of Sister J Woodward her staff Messrs May & Baker supplied the hydrox *bamidine*

Addendum

Since submitting this report for publication we have tre *a third infant suffering from thrush* œsophagitis, incoördi tion of swallowing, and aspiration pneumonia The c was 3 weeks old Hydroxystilbamidine was given slo over two to three hours by continuous intravenous drip a scalp vein The compound was *given twice* daily for *days* No thrombophlebitis occurred and we were abl use the same vein throughout this period The *baby* an excellent and rapid recovery

REFERENCES

Adams J M (1944) *J Pediat* 25 309
Amlie R (1952) *Ann paediat* 179 316
Anderson N A Sage D N, Spaulding E H (1941) *Amer J D Child* 67, 450
Ardran, G M, Kemp F H (1952) *Brit J Radiol* 25 406
Ashley, J N, Harris J O (1946) *J chem Soc* 2 567

References continued at foot of next column

THE USE OF ACETAZOLEAMIDE IN ACUTE RESPIRATORY ACIDOSIS

MARY WISHART
B.Sc., M.B Glasg
HOUSE PHYSICIAN

BERNARD ISAACS
M.B Glasg F.R.F.P.S D Obst
REGISTRAR

STOBHILL GENERAL HOSPITAL, GLASGOW

The heterocyclic sulphonamide 2 acetylamino 1 3 4 iadiazole-5-sulphonamide (acetazoleamide Diamox, derle), inhibits the enzyme carbonic anhydrase, its ain pharmacological effect being exerted on the renal bule cells (Miller et al 1950 Berliner et al 1951) ading to increased urinary excretion of sodium tassium, and bicarbonate reduced excretion of monium ion, a rise in pH of the urine and a fall in the um-bicarbonate level and in pH of the blood (Nadell 53 (ounihan et al. 1954)

The treatment of respiratory acidosis with acetazole ide was suggested by Nadell (1953) who obtained vourable results in 6 cases Similar results were tained by Heiskell et al (1954) in 4 ambulant patients th pulmonary emphysema and by Ruskin (1955) in case of cor pulmonale

The rationale of this therapy was elaborated by Nadell 953). She found in 2 controls and in 5 of 6 patients th respiratory acidosis that when acetazoleamide was t given both the serum bicarbonate level and the I of the serum fell with continued therapy the pH urned to normal but the serum bicarbonate level mained low This must have been due to a fall in the tial pressure of carbon dioxide in the blood (pCO_2) duced by respiratory compensation for the metabolic dosis. Nadell commented that pulmonary dissipation carbon dioxide seemed to be more effective after the ministration of acetazoleamide but the mechanism s obscure

Some criticism of this argument might be advanced spiratory acidosis the respiratory centre is already tively insensitive to the stimulus of a high pCO_2 ventilatory function of the lungs is so impaired that olar loss of carbon dioxide cannot be significantly eased despite additional stimulation of the respiratory tre (Wilson et al. 1954 Cohn et al 1954) and urinary of bicarbonate in response to the administration of acetazoleamide would tend to alter the ratio of serum bicarbonate to pCO_2, with a fall in pH which is potentially harmful to a patient who is already acidotic

Despite these theoretical objections we have given acetazoleamide to 3 patients with acute respiratory acidosis in the hope of preventing or relieving carbon dioxide narcosis. The patients all had chronic bronchitis emphysema and pulmonary heart-disease and their symptoms had been severely aggravated by acute respiratory infection. Striking biochemical changes took place in all the patients after the administration of acetazoleamide but no clinical improvement was noted Judged clinically the condition of the 1st patient was deteriorating before acetazoleamide was given the drug did not influence the course of the disease and the patient died In the 2nd patient the administration of acetazoleamide was immediately followed by much clinical deterioration a rapid downhill course ending in death The 3rd patient showed an alarming deterioration of the clinical condition after a single dose of acetazoleamide but improved when the drug was withheld

Case reports

Case 1—A woman aged 59 was admitted to hospital with a severe acute respiratory infection She had chronic bronchitis of five years duration, and this was now accompanied by emphysema and pulmonary heart-disease On admission she was pyrexial, dyspnoeic and cyanosed but conscious and rational.

Treatment and Course—She was treated with penicillin digitalis, and mersalyl and oxygen was given in small amount by nasal catheter with relief of cyanosis. Next day her general condition gradually deteriorated and she became comatose Her optic fundi showed gross distension and tortuosity of veins and congestion of the optic discs. Her serum bicarbonate level was 37 8 m.eq per litre and her serum urea level was raised but her serum potassium level was normal and remained so throughout the illness. She was given acetazoleamide 500 mg on the day after admission and the same dose was given daily for the next three days, and then every second day for three more doses. Eighteen hours after the first dose of acetazoleamide the serum bicarbonate level had fallen to 29 7 m.eq per litre but no clinical improvement was noted The serum bicarbonate level in the next ten days ranged from 32 4 to 41 8 m.eq per litre Oxygen therapy was continued by intermittent use of the oxygen tent and oxytetracycline was given The patient remained critically ill, with pyrexia dyspnoea and drowsiness, and four weeks after admission she lapsed into coma and died

Necropsy showed chronic bronchitis, emphysema recent bronchopneumonia right ventricular enlargement and congestive cardiac failure

Case 2—A woman aged 63 with nine years history of chronic bronchitis, was admitted to hospital with an acute exacerbation of pulmonary heart disease following an infection of her upper respiratory tract On admission she was cyanosed and dyspnoeic but conscious and rational

Treatment and Course—Penicillin and digitalis were administered but oxygen was at first withheld On the day after admission the serum bicarbonate level was 36 0 m.eq per litre The optic fundi showed dilatation and tortuosity of the veins, and the discs were slightly swollen. Oxygen therapy was started by nasal catheter and acetazoleamide 500 mg was given. Twenty four hours later the serum bicarbonate level had fallen to 32 4 m eq per litre and in that period the patient excreted 705 ml of urine containing 31 5 m.eq of bicarbonate On the second day after admission the patient became drowsy and confused and was placed in an oxygen tent She was given acetazoleamide 500 mg twice on that day and once more on the third day the serum bicarbonate level then having risen again to 30·0 m eq per litre The serum potassium level was normal Her condition rapidly deteriorated the drowsiness deepened into coma and she died on the third day after admission

Necropsy showed chronic bronchitis and recent pneumonic lesion fatty infiltration of and enlargement of the right ventricle cerebral oedema but no local lesion in the

Case 3—A woman aged 60 with chronic bronchitis with emphysema a

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DR. WOLFF AND OTHERS: REFERENCES—continued
r R. (1955) *Brit J Radiol* 28 [illegible]
h *Medical Journal* (1950) ii, 1430
rd, P J., Hargreaves, W H (1947) *Lancet* ii 686
r J (1954) *Arch. intern Med* 93, 798
ls, C. C. Bocobo F C, Harrell E. R Block W D (1954) *U.S. Forces med J* 5 919
J Nenna A, Berry H (1954) *Blood* 9 696
J H (1938) *Arch Dis. Childh* 13 211
n, J D (1941a) *Ann trop Med Parasit* 35 78
(1941b) *Ibid* p 147
mann, E., Rinker, I (1950) *Ann paediat* 175 1
A A (1954) *J Bone Jt Surg*, 36A, 850
A (1953) *Arch Dis. Childh* 28 412
r H., Todd R. M (1949) *Ibid* 24 [illegible]
ham, G H, Henderson J L (1942) *Lancet*, i 64
r L. E., Sen Gupta P C (1942) *Indian med Gaz.* 77 71
ski W (1953) *Dtsch med Wschr* 78 333
nbach L. B., Greenspan, E. M (1948) *Medicine Baltimore* 27 327
arz, J., Adriano S (1953) *J. invest Derm* 20 [illegible]
n Gupta, P. C. (1949) *Lancet* ii, 97
ith, D T (1953) *GP (Kansas City Mo.)* 8 69
per I (1945) *J Mt Sinai Hosp.* 15 150
— (1952) *Amer J Med* 13 655
— Lieben, F., Greenspan E. Schneid B (1951) *Cancer* 4 1210
— McVay, L. V. (1953) *Amer J Med* 15, 603
— Schneid B., McVay L., Lieben I (1954) *Trans N Y Acad Sci* 14 269
lotowsky M., Ironson, E. J Gregory I J Winsten S (1954) *tibiot. Chemother.* 4 165
tani M., Dameshek, W (1953) *Lancet* ii [illegible]
ng, W, D., Kyle J W Hobson J L (1954) *Ann. intern Med* 41 86
inberg H J., Lawrence C H., Buchholz, A (1954) *Arch intern Med.* 94 103

disease, was moderately ill when admitted for treatment of an acute respiratory infection.

Treatment and Progress —She improved under treatment with penicillin, digitalis, and oxygen given by nasal catheter Her serum bicarbonate level on admission was 49 5 m eq per litre, the level fell to 38 3 m eq per litre next day, but rose on the third day to 40 5 m eq per litre Acetazoleamide 500 mg was given on the third day In the next twenty four hours the patient excreted 1055 ml of urine containing 100 m.eq of bicarbonate, and the serum-bicarbonate level fell to 36 9 m eq per litre No more acetazoleamide was given, but renal excretion of bicarbonate continued for two more days, a further 62 m.eq of bicarbonate being excreted. This was accompanied by a further fall in serum bicarbonate level to 34 2 m eq per litre and 30 6 m eq per litre two and three days respectively after the administration of acetazoleamide Twenty four hours after the acetazoleamide had been given there was an unexpected serious deterioration in the patient's clinical condition respiration became shallow, cyanosis increased, and she became extremely drowsy She was placed in an oxygen tent, where she remained drowsy, confused, and breathless for two days, and then gradually improved During this time the physical signs in the chest were unchanged, the retinal veins were tortuous and congested, but there was no papillœdema, and the serum potassium level was normal Oxygen therapy was discontinued after three days, and the patient eventually made a good recovery The serum bicarbonate level was estimated every second day in the next week as 38 7, 32 0, and 37 8 m.eq per litre

Discussion

The clinical deterioration in these 3 patients depended on a combination of toxæmia, hypoxia, and retention of carbon dioxide Toxæmia played an important part in case 1, but in the 2 other patients the infection responded initially to treatment with an antibiotic Anoxia was present in all the patients, and our policy was to relieve this gradually, following the advice of Simpson (1954) by giving oxygen at first by nasal catheter at a rate of flow of 2–4 litres a minute, and only later transferring the patients to an oxygen tent Retention of carbon dioxide was probably a major factor leading to deterioration, and oxygen therapy may have contributed to this

In any attempt to measure the effects of retention of carbon dioxide the relevant physiological observations are the alveolar concentration of carbon dioxide and the pH of the serum, from which can be determined the pCO_2 It is unfortunate that it was impossible to obtain these measurements in our patients The serum bicarbonate level gave no indication of the clinical condition Case 2 was very much more ill, with an initial serum-bicarbonate level of 36 0 m eq per litre, than was case 3, whose serum-bicarbonate level on admission was 49 5 m eq per litre Considerable fluctuations in the serum-biocarbonate level in case 3 have already been noted, these were independent of treatment and unrelated to the clinical condition There seems to be no doubt, however, that acetazoleamide caused an initial fall in the serum-bicarbonate level in all 3 patients The lack of clinical improvement suggests that the fall of the serum-bicarbonate level was not accompanied by a corresponding fall in pCO_2, presumably because of pulmonary insufficiency We cannot offer direct proof of this hypothesis, but, if it is true, the initial effect of acetazoleamide in these patients was to alter the ratio of pCO_2 to serum-bicarbonate in such a way as to cause a potentially dangerous fall in serum pH There is ample evidence that this happens when acetazoleamide is administered to patients with normal respiratory function (e g, Nadell 1953, Counihan et al 1954), and Simpson has demonstrated that the same mechanism operated in his own cases of respiratory acidosis The rapid return of the serum bicarbonate level to its initial high value in cases 1 and 2 was not accompanied by improvement, possibly bec respiratory centre remained adversely affected by the persistently high pCO_2, or as a result of temporary lowering of pH

We conclude that in these 3 cases of acute r acidosis accompanied by pulmonary infection acetaz amide was of no value, and that its property of prom ing renal excretion of bicarbonate may have been har to the patients

Summary

The carbonic anhydrase inhibitor, acetazoleamide, given to 3 patients with acute exacerbation of respiratory acidosis

Increased urinary excretion of bicarbonate and of the serum bicarbonate level resulted

In all 3 cases there was clinical deterioration 2 patients died, and the 3rd recovered when the amide was withheld

It is concluded that acetazoleamide may be de in acute respiratory acidosis

We wish to thank Prof Stanley Alstead and Dr J Macarthur, under whose care these patients were treated, their advice and encouragement, and Dr J W and Dr A W Mollison for the biochemical estimations.

REFERENCES

Berliner, R W, Kennedy, T J jun, Orloff, J (1951) *Amer J* 11 274
Cohn, J E, Carroll D G, Riley, R. L (1954) *Ibid* 17, 44
Counihan, T B, Evans, B M., Milne, M. D (1954) *Clin Sci.* 13
Heiskell, C L jun Belsky, J B, Klaumann, B F (1954) *J A med Ass* 156 1059
Miller, W H, Dessert, A M, Roblin, R O jun (1950) *J A chem Soc* 72 4893
Nadell J (1953) *J clin Invest* 32, 622
Ruskin, A (1955) *Arch intern Med* 95 24
Simpson, T (1954) *Brit med J* 1, 297
Wilson, R H, Hoseth, W, Dempsey, M. E (1954) *Amer J* 17, 464

TUBERCULIN AND LEPROMIN SENSITIVITY IN THE SOUTH AFRIC BANTU

A PILOT SURVEY

S W A Kuper
M B Rand, D P H., D T M & H, D C.P
CLINICAL PATHOLOGIST, BROMPTON HOSPITAL, LOND

It has often been stated that skin sensitivit tuberculin and lepromin are correlated, and it has inferred that this reflects an immunological relati (Chaussinand 1950, Fernandez 1943, Lowe and Mc 1953b)

The significance of skin sensitivity to lepromin clearly established, and this sensitivity is used as an to classification and prognosis in leprosy rather than a means of diagnosis Most patients with lepromat leprosy are relatively insensitive to lepromin, where those with tuberculoid leprosy are said to show a m marked allergic response, which may be either a "tub culin like" reaction at forty-eight to seventy two ho (the Fernandez test) or an indurated nodule from two five weeks after the inoculation The two types of rea tion are said to parallel one another in the individ case (Fernandez 1940, Lowe and McNulty 1953b), but th method of preparation of the antigen determines wheth the early or the late reaction is the greater Much of th published material on this subject is largely speculati but a good deal of the data appears to support the the that the degree of correspondence between tuberc and lepromin reactions is far greater than could accounted for if the two forms of sensitivity were com pletely unrelated

I describe here an attempt to elucidate some of the problems by tests on South African Bantu patients controls Patients with pulmonary tuberculosis others with leprosy were investigated together with apparently healthy adults The numbers tested were

TABLE I—MEAN SIZES OF REACTIONS

Group	No of persons	Mean transverse diameter of reaction (standard error of mean)					
		Tuberculin at 48 hr	Nil reactors	Lepromin at 48 hr	Nil reactors	Lepromin at 4 weeks	Nil reactors
ntrols (adult males)	105	12 5 mm. (*0 48*)	0	3 8 mm (*0 24*)	8	3 7 mm. (*0 15*)	1
berculosis (adult males)	53	14 1 mm (*0 79*)	1	7 4 mm (*0 77*)	2	5 9 mm (*0 30*)	1
promatous leprosy (adult males)	33	16 5 mm (*3 18*)	1°	3 4 mm (*0 43*)		1 5 mm. (*0 24*)	13
promatous leprosy (adult females)	15	21 0 mm (*0 53*)	1	2 5 mm (*0 31*)	–	0 7 mm (*0·19*)	7
berculoid leprosy (adult males)	25	10 6 mm. (*1 14*)	3	15·0 mm (*1 41*)		7·2 mm (*1 19*)	2
berculoid leprosy (adult females)	12	5 0 mm (*1 22*)	2	8 8 mm (*1 60*)		5 8 mm. (*1 31*)	1
berculoid leprosy (male children)	7	6 0 mm (*3 20*)	3	11 6 mm (*3 56*)		5 4 mm (*2 11*)	2
berculoid leprosy (female children)	6	3 2 mm (*1 44*)	2	10 2 mm. (*3 12*)		6·2 mm (*2 36*)	

This table represents the mean transverse diameters of reactions recorded in all the groups of patients It lists the reactions to tuber- in at 48 hours, and to lepromin at 48 hours and at 4 weeks The standard error of the mean is included in parentheses after each result e numbers of subjects in whom no reaction was found are given in a separate column, but they are included in the figures of totals for h group

ge but it was hoped that this disadvantage would be ercome by careful standardisation of methods (Guld d Rud 1953 Meyer et al 1951)

Methods

The persons tested were divided into three categories

Group 1—Patients with pulmonary tuberculosis (37 adult les)

Group 2—Patients with leprosy (102 mostly adults but me children aged 10–16 years)

Group 3— Controls (114 adult males)

The patients with tuberculosis were in hospital during e trial. They showed no obvious evidence of leprosy diographs of the chest were characteristic of pulmon y tuberculosis, and tubercle bacilli had been isolated m the sputum in about 90% of the cases

The leprosy patients were all being treated in an stitution during the trial, and radiological examination thin the preceding few months showed no evidence of lmonary tuberculosis The clinical diagnosis of leprosy d in all cases been substantiated by examination of ne smears and the type of leprosy was classified by e experienced permanent medical staff of the institute ts were made in 52 patients with lepromatous leprosy d 50 with tuberculoid leprosy

The controls consisted entirely of adult industrial ployees working in a soap factory and resident in the y Within a few weeks of the start of the trial they were diographed to exclude anyone with a shadow suggesting lmonary tuberculosis No obvious evidence of leprosy s seen in any member of the group

So far as is known none of the persons in any group d ever received B C G vaccine

chniques

Dried lepromin of the Dharmendra type was prepared by . N Figueredo of the Acworth Leprosy Home Bombay his antigen produces more prominent early reactions than layed ones, and is therefore more strictly comparable to berculin than is the Mitsuda type of antigen. The lepromin s finally suspended in half the recommended volume of line solution to reduce the volume of the intradermal injec n from 0·2 ml to 0 1 ml It was sealed in ampoules in reat Britain and was used within a month of the date of lling

Tuberculin was used in the form of purified protein rivative It was dissolved and diluted so that 0 1 ml ntained 5 tuberculin units. It was thought that this small se of tuberculin would detect only high specific degrees of sitivity (Palmer and Bates 1952 Palmer 1953) Tablets re dissolved freshly for each session of inoculations.

Syringes were of the all glass tuberculin type All the ringes were new and each was used for only one inoculating ssion to prevent possible transference of antigen Only new edles were used and they were discarded at the end of each ssion. The syringes were examined for leakage and the iteria recommended by Guld and Rud (1953) for field trials re adopted 48 syringes were tested by their method but ly – satisfied their requirements. Fortunately it was found that a light smear of silicone oil applied to the barrel of the syringe reduced leakage to such a degree that 37 out of 48 syringes could be used Several intradermal inoculations of water made with these syringes in hospital staff produced no evidence of sensitivity to the silicone oil

Procedure

All the inoculations and readings of results were made by me to minimise individual variations of judgment (Meyer et al 1951) All the controls were inoculated on one day and all the patients with leprosy and tuberculosis on another The injections were made in the skin of the ventral surface of the forearm about half way between the wrist and elbow The volume inoculated was in all cases 0 1 ml administered intradermally so as to raise a distinct bleb in the skin Lepromin was injected into the left arm and tuberculin into the right each patient received the two inoculations within a few minutes

Because of skin pigmentation in the patients no attempt was made to delimit areas of erythema Measurements were made of the induration produced the edges of the areas were carefully defined, and the transverse diameters measured in millimetres with a transparent rule The site of inoculation of the tuberculin was examined after forty eight hours that of the lepromin inoculation was examined at forty eight hours, and after one two three, four five and six weeks

Results

Table I shows that the tuberculous and the control groups consisted entirely of adult males, but the leprosy patients included adults and children of both sexes Distinct variations are apparent between males and females and adults and children so the results are recorded under separate headings In figs 1–3 the sexes and ages are not separated

The numbers of subjects vary slightly from table to table depending on the numbers available for measurement on the day in question The controls for example were 114 after forty eight hours but only 105 of these presented themselves for examination on the twenty eighth day

The results may be examined in one of two ways In the first place evidence may be sought of any correlation between skin sensitivities to lepromin and tuberculin This is best elicited statistically by the examination of product moment correlations but dot diagrams give an approximate picture of the relationships (fig 1) (The product moment correlation takes into account the sizes of reactions in each patient and may be regarded as a statistic summarising the degree of association exhibited in the dot diagrams) In this investigation no correlation between the two forms of sensitivity was found in 105 controls nor was there any evidence of association in the 86 adults with leprosy In the 53 patients with pulmonary tuberculosis, however a definite positive correlation was obtained (product moment correlation=0·40 ** The chance of this being a random result is less

1000) * A small positive correlation was also found between the tuberculin reactions at forty-eight hours, and the lepromin reactions at twenty-eight days It is smaller than the forty-eight-hour correlation, and possibly merely residual from it The need for caution in assessing the importance of the observation is emphasised by the failure to find any correlation between the tuberculin and lepromin reactions in the other two test groups

The results may also be examined in another way If the suggestion is accurate that there are antigens common to the tubercle and leprosy bacilli, one might expect to find skin hypersensitivity in each of the two diseases, to the causal organism of the other, or to products derived from it Patients with tuberculosis might react strongly to lepromin injection, and patients with leprosy to tuberculin This could never be more than an approximation, however, for lepromin hypersensitivity is far less regular, even in leprosy, than is tuberculin sensitivity in tuberculosis

Skin reactions to lepromin (examined at forty-eight hours) were compared in healthy adults and in patients with pulmonary tuberculosis The latter were found to be significantly more sensitive to lepromin than the controls (mean for tuberculous patients 7 4 mm , and for controls 3 8 mm), and the same trend is evident in histograms (fig 3) †

Conversely, skin reactions to tuberculin were compared in healthy adults and in patients with leprosy The picture is rather complex Patients with tub leprosy appear to react less strongly to tuberculin th do the normal controls (fig 2) This difference is siderably reduced, however, if the male patients are compared with the controls, all of whom were ma The mean size of reactions in the male patients wi tuberculoid leprosy was 10 6 mm , and that in the nor controls 12 5 mm The difference is not significant Th female leprosy patients cannot properly be compa with the male controls In lepromatous leprosy, th measurements are widely scattered , the mean reacti however, are significantly greater (males, mean=1 mm) despite the fact that 12 members of this gro showed no reactions at all to tuberculin (fig 2) The was a very high degree of tuberculin sensitivity in som members of this group

Much of the published work on skin reactions in lepros records the observed reactions in terms of an arbitrar scale of "positive" and "negative" reactors. So

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* *Validity of Tests Used*—In comparing mean sizes of reactions between the various groups, and in assessing the significance of correlation between the reactions obtained to the two antigens, statistical tests were used which depend for their validity on the normal (gaussian) distribution of the measurements Evidently this type of distribution is not fulfilled, so the tests must be regarded as having only an approximate significance

† In figs 2 and 3 data relating to the forty eight hour tubercu and lepromin reactions are shown as histograms. The gr intervals have been judiciously chosen to conceal th tendency towards recording even numbers of millimetr particularly in measuring the relatively large reacti Superimposed on the histograms of the controls are th fitted logarithmic normal distributions, reached disregarding the information on reaction diameters than some arbitrarily selected level—8 mm in the c of tuberculin reactions, 1 5 mm in the case of lepro reactions (Hald 1952a and b)

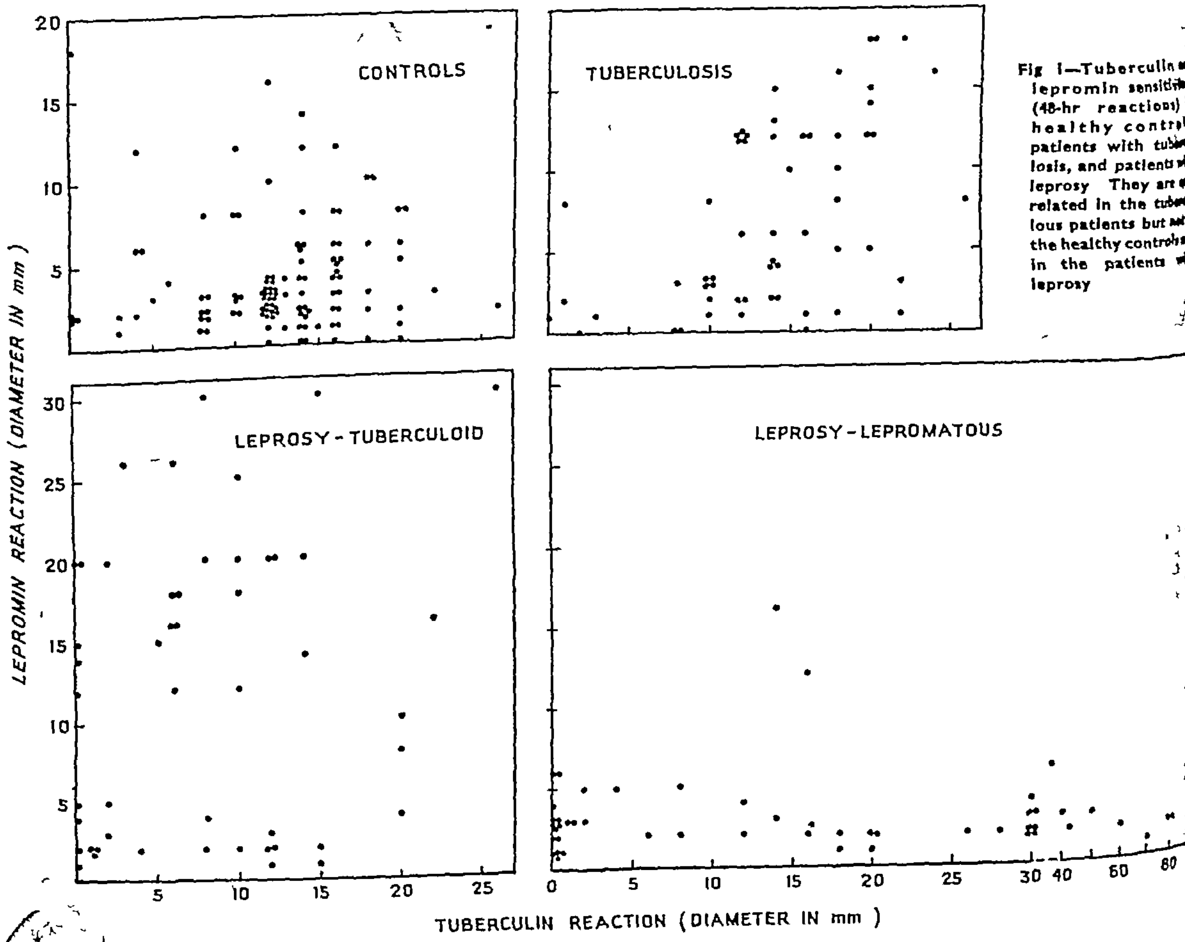

Fig 1—Tuberculin lepromin sensiti (48-hr reactions) healthy controls, patients with tu losis, and patients leprosy They are related in the tu lous patients but the healthy controls in the patients leprosy

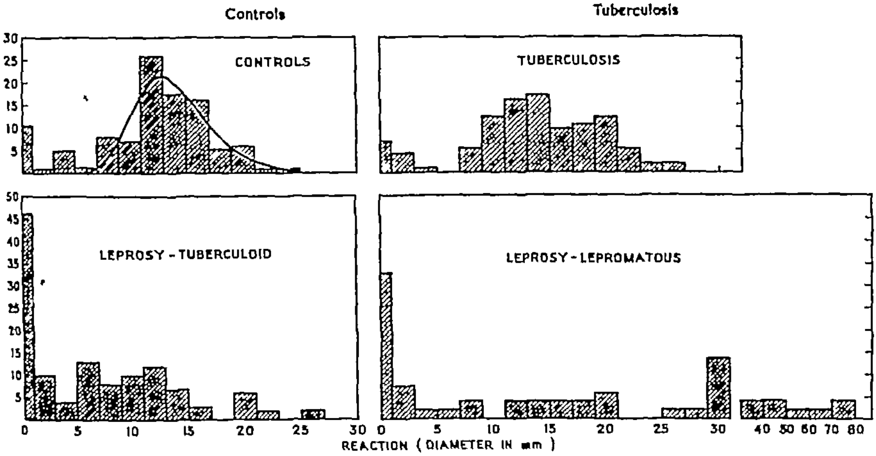

Fig 2—Tuberculin sensitivities (48-hr reactions) in healthy controls patients with tuberculosis and patients with leprosy

ndards provide a useful rule of thumb for clinical rposes but their adoption in a survey of immunological actions leads to the discarding of a great deal of the formation (Edwards et al 1953) This trial records the tual observed measurements but it is possible to divide e readings at any desired level to facilitate comparison th results published only in terms of 'positives' and negatives' Such comparison is obviously of limited lue unless conditions in the two surveys are very nilar

Table II represents the results of this trial analysed the above lines Tuberculin reactions with a diameter 6 mm or more are corded as positive lepromin reac ons 6–10 mm. in ameter as 'doubtful' and 11 mm or ore as positive hese criteria for rty eight hour promin reactions ere recommended y the International eprosy Congress in adrid 1953) In ble II doubtful d "positive" results re grouped together y this method of nalysis the results are gnificant only if it an be shown that he likelihood of the bserved distributions aving occurred by hance is less than /20 This level of gnificance was not ttained by any of the roups in this series.

Despite the possi ility of errors in lassification between he types of leprosy he results for the two groups are not 'combined' for any of the investigations This precaution was deemed necessary because of the widely divergent patterns of skin sensitivity in the two forms of leprosy It may be argued that the clinical classification was possibly biased by the results of earlier lepromin reactions but the pictures of tuberculin sensitivity in the two forms of leprosy are so widely different that it appears to reduce to a minimum the likelihood of widespread misclassification of the type of disease.

Early and Late Lepromin Reactions

The forty-eight-hour lepromin reaction is not significantly different in controls and in patients with lepro

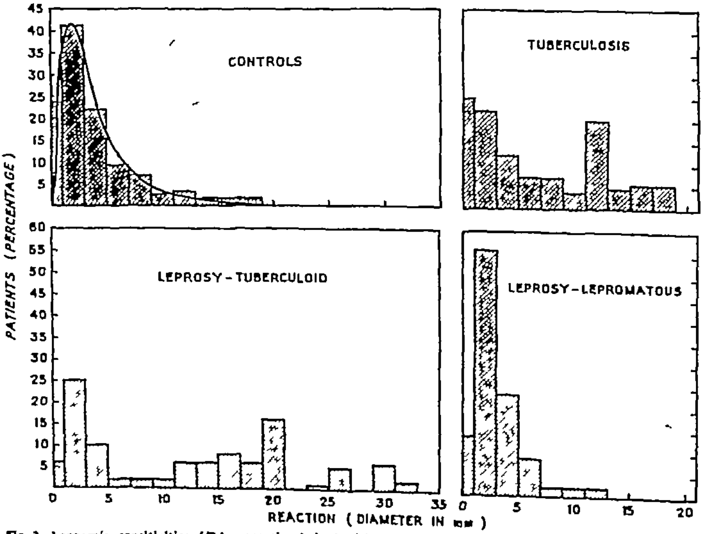

Fig. 3—Lepromin sensitivities (48-hr reactions) in healthy controls, patients with tuberculosis and patients with leprosy

TABLE II—NUMBERS OF "POSITIVE" AND "NEGATIVE" REACTORS

Group	Tuberculin negative (0–5 mm)		Tuberculin-positive (≥6 mm)		Total
	Lepromin negative (0–5 mm)	Lepromin positive or doubtful (≥6 mm)	Lepromin negative	Lepromin positive or doubtful	
Controls	8	4	80	22	114
Tuberculosis	4	1	24	28	57
Lepromatous leprosy (males)	12	1	17	3	33
Lepromatous leprosy (females)	6	2	11	0	19
Tuberculoid leprosy (males),	3	4	7	18	32
Tuberculoid leprosy (females)	7	4	3	4	18

The subjects tested are grouped in this table into "positive" and "negative" reactors, in terms of arbitrary scales, as defined.

matous leprosy, but late lepromin reactions tend to be smaller in the latter This difference may be due to inaccuracy in measuring the very small reactions In males with lepromatous leprosy there is a 90% probability that the mean twenty-eight day reaction size lies between 0 9 mm and 2 1 mm, whereas for controls at twenty-eight days the equivalent figures are 3 4 mm and 3 9 mm (table I) In adult males with tuberculoid leprosy the late lepromin reaction, as would be expected, is substantially greater than that seen in controls (mean twenty-eight day lepromin reaction 4 8–9 6 mm)

Skin reactions to both antigens in males with tuberculoid leprosy are usually larger than in females (table I) This is particularly true of the forty eight-hour tuberculin reaction This sex difference is not so clear cut in lepromatous leprosy, unless one omits the 12 males and 1 female showing no measurable reactions to tuberculin, and the 13 males and 7 females showing no reaction to lepromin at twenty eight days If a measurable reaction does result, the mean values are larger in males At twenty-eight days the trend is still present but less striking

There is some correlation between forty eight hour and twenty-eight-day lepromin reactions, but, except in the case of tuberculoid leprosy, it is smaller than might be expected (Fernandez 1940) The two reactions were not always parallel, and an appreciable late reaction was usually (but not always) preceded by a large early reaction In view of the type of antigen used, this feature is perhaps not surprising, and no emphasis can be placed on the late readings

It might prove useful to investigate late lepromin reactions on the basis of histological appearances in biopsy material from the site of inoculation This technique has been found to increase the diagnostic value of reactions to Nickerson-Kveim antigen in sarcoidosis (Siltzbach and Ehrlich 1954)

Discussion

In an investigation of this kind there are several difficulties in interpreting the results It has been claimed that tuberculin and lepromin sensitivities are positively correlated, and on the basis of this observation an immunological relationship between tuberculosis and leprosy has been postulated Such a thesis would be more easily tenable if the sensitivities involved indicated immunity in their respective diseases, but tuberculin sensitivity does not imply immunity to tuberculosis, and significant lepromin sensitivity is seen mainly, if not [illegible], in the tuberculoid form of leprosy The re[illegible] be regarded as immunological factors only in so far as they reflect the capacity of the host's tissues to react to the corresponding antigens

In tuberculoid leprosy, skin sensitivity to lepromin is usually high, the disease itself is mild and self limiting, suggesting a high resistance to leprosy bacilli From these observations it appears to have been inferred that high lepromin sensitivity is closely associated with high resistance, and, therefore, the production of lepromin sensitivity in uninfected people might protect them against infection For this purpose, B C G vaccination has been advocated Many workers have recorded increases in lepromin as well as tuberculin sensitivities after the administration of B C G vaccine to healthy subjects A large proportion of people with "negative" reactions to lepromin are stated to become "positive" after this measure (de Souza Campos 1953, Ferna 1943, 1951, Kocsard and Sagher 1953, Lowe and Mc 1953a) This observation is particularly intere Cochrane (1955) states that lepromin "conversion" i seen in patients with lepromatous leprosy who tuberculosis

The present investigation is not concerned with relationship of immunity and skin sensitivity, but with the possibility of there being some correlation between the sensitivities induced in man by infection with tubercle and with leprosy bacilli In this pilot study the degree of correlation established between tuberculin and lepromin sensitivities was small, and was found only among the patients with pulmonary tuberculosis, the smallest of the three groups tested in the trial Furthermore the tuberculous patients showed a greater degree of sensitivity to lepromin than did the controls—though this may be merely a consequence of the former correlation In lepromatous leprosy, where lepromin sensitivity is slight or absent, a small proportion of the patients showed an intense degree of sensitivity to tuberculin. When these were excluded the two main groups of leprosy patients did not show greater tuberculin sensitivity than the controls

In view of these findings there seems to be no simple and direct relationship between tuberculin and lepromin sensitivities However, the observations in patients with tuberculosis and lepromatous leprosy suggest the existence of a relationship of some kind

Summary

A pilot survey was made to investigate correlation between tuberculin and lepromin sensitivities in the South African Bantu

Three test groups were selected for the trial 10 patients with leprosy, 57 patients with pulmonary tuberculosis, and 114 healthy controls

In the controls and in the patients with leprosy no correlation could be established between lepromin and tuberculin sensitivities In the patients with pulmonary tuberculosis, however, a positive correlation was found. Furthermore these tuberculous patients showed a greater degree of sensitivity to lepromin than did the controls

A small proportion of the patients with lepromatous leprosy showed a very high degree of sensitivity to tuberculin

I am greatly indebted to the medical superintendents and staff of the Westfort Institution, Pretoria, and the Waterval Hospital, Johannesburg, for facilities and willing assistance, to the British Tuberculosis Association for providing the lepromin, and to Dr R G Cochrane, through whose kind services it was made available, to Mr B Benjamin for his advice in planning the trial and for scrutinising the early results, to Mr P M Payne for his exhaustive statistical analyses of the complete findings, and to the Board of Governors of the Brompton Hospital for allowing a period of study leave during which this work was done Lastly, I should like to thank Dr R W Riddell and Dr J R Bignall, of the Brompton Hospital, for their advice, help, and encouragement

References at foot of next column

TRAUMATIC RUPTURE OF DIAPHRAGM WITH HERNIATION OF ABDOMINAL VISCERA

K. K. SINHA
F.R.C.S.

[illegible]

Indirect violence is one of the rarer causes of traumatic rupture of the diaphragm, and in most recorded cases the patient sustained gross injury to abdominal viscera. In the case described here the only abdominal organ to be injured was the spleen.

A woman, aged 45, was admitted to hospital a few hours after a car accident in which she had been thrown on to her left side and had felt a sudden snap all over the left side of her chest.

On admission her pulse-rate was 90 per min., blood pressure 120/90 mm. Hg, respirations 20 per min. There was no cyanosis or evidence of respiratory distress, though she complained of pain in the left side of her chest. Bowel sounds were audible over the left hemithorax.

Radiography of the chest revealed fractures of the upper [illegible] ribs on the left side. The left lung seemed to be collapsed and the diaphragm appeared unusually high; the gastric shadow could be seen as high as the fifth left intercostal space (fig 1). Barium-swallow showed considerable distortion of the oesophagus and confirmed the presence of stomach high up in the thoracic cavity (fig 2).

Diagnosis.—The absence of respiratory distress was difficult to explain in view of the radiographically and clinically demonstrable collapse of the left lung. The problem was whether it was a case of congenital high diaphragm or a tear of the diaphragm with herniation of the bowel and collapse of the lung. The history of trauma along with the radiographic findings suggested a diagnosis of traumatic rupture of the diaphragm.

Progress.—The patient's general condition remained quite satisfactory. She had no difficulty in taking food, and the bowels continued to act normally for two days after admission. On the third day she started to vomit, and screening showed the beginning of [illegible]. She was [illegible] in the thorax [illegible]

Operation.—Thoracotomy was [illegible] through the bed of the [illegible]. Inside the left pleural cavity the spleen, stomach, transverse colon, [illegible] were found. On the left side there was a large tear [illegible] backwards, where the [illegible] the muscular portion. The spleen was [illegible] but there was no [illegible] to suggest [illegible] bleeding. But on opening the chest profuse [illegible] began and splenectomy had to be done. The stomach was returned to the abdomen and the [illegible] was [illegible]. The diaphragm was repaired with interrupted [illegible] sutures, and after the abdominal and thoracic [illegible] had been evacuated the lung expanded without any difficulty [illegible] by the anaesthetist.

Fig. 1—Radiograph of chest showing high gastric shadow, collapsed left lung, and fractured ribs.

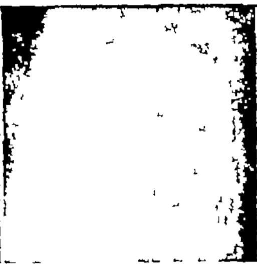
Fig 2—Barium-swallow: oesophagus distorted and the stomach high in the thoracic cavity.

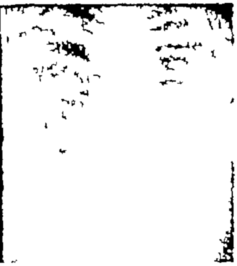
Fig 3—Postoperative appearance: left lung re-expanded.

Progress.—Postoperative progress was uneventful, and bowel sounds returned within twenty-four hours. Oral fluids were begun within thirty-six hours of operation. On the tenth day after operation the blood-pressure was 120/80 mm. Hg, and the apex-beat had returned to the normal position. There was no abdominal distension. Breath sounds were clearly audible at the left base though slightly diminished compared with the opposite side. Radiography showed satisfactory expansion and functioning of the left lung (fig 3).

Noteworthy features in this case were that: (1) the patient's general condition remained good despite collapse of one lung and herniation of a large amount of bowel; (2) there was no evidence of shock at the time of admission; and (3) the ruptured spleen bled only when the chest was opened.

DR KUPER: REFERENCES

Aravelman, I. R. (1950) *Int. J. Leprosy*, 18, 441.
Cochrane, R. G. (1951) Personal communication.
de Souza Campos, N. (1953) *Int. J. Leprosy*, 21, 307.
Edwards, L. B., Palmer, C. E., Magnus, K. (1953) B C G Vaccination. World Health Organisation Monograph Series no. 1. Geneva.
Fernandez, J. M. M. (1940) *Int. J. Leprosy*, 8, 1.
— (1943) *Ibid*, 11, 15.
— (1951) *Ibid*, 19, 474.
Hald, J., Rud, C. (1953) *Brit. med. J.* i, 368.
Hald, A. (1952a) Statistical Tables and Formulæ. New York.
— (1952b) Statistical Theory and Engineering Applications. New York.
Kooij, R., Gerber, F. (1953) *J. invest. Derm.* 21, 69.
Lowe, J., McNulty, F. (1953a) *Int. J. Leprosy*, 21, 173.
— — (1953b) *Brit. med. J.* ii, 579.
Meyer, S. N., Hougen, A., Edwards, P. (1951) *Publ. Hlth Rep., Wash.* 66, 561.
Palmer, C. E. (1953) *Amer. Rev. Tuberc.* 68, 678.
— Bates, L. E. (1952) *Bull. World Hlth Org.*
Rosenbach, L. E., Ehrlich, J. C. (1951) *Amer. J.* [illegible]

DIAPHRAGMATIC HERNIA FOLLOWING INJURY

F. A. HAMDI
M.B. Alexandria, Ph.D. Edin.

D. K. STURDY
M.B. Lond.

REGISTRARS, DEPARTMENT OF NEUROSURGERY, MORRISTON HOSPITAL, SWANSEA

It is known that severe crushing injuries to the abdomen and chest may be responsible for rupture of the diaphragm with subsequent development of diaphragmatic hernia. Of 7 cases reported by Evans and Simpson (1950) 5 were due to severe crushing injury to the abdomen, 1 sustained bruising of the chest wall, and none had fractured ribs. Evans and Simpson suggested that the mechanism of the injury to the diaphragm was in the nature of an explosive rupture due to sudden increase in intra-abdominal pressure.

The case presented here illustrates how herniation of abdominal contents into the thoracic cavity revealed itself as an acute abdomino-thoracic emergency twenty-four hours after the injury.

Case report

A man, aged 40, was admitted semiconscious to the neurosurgical unit at 11.30 P.M. on May 8, 1951, having been knocked down by a motor-car an hour previously. Immediately after the accident he had been given morphine gr. [illegible] by a [illegible] practitioner.

On admission he was easily roused but did not [illegible]. He had a laceration over the right eye [illegible] skull showed a comminuted fra

Dr. Robert Heilig
S. M. S. Medical College
33355
JAIPUR

right superior and lateral orbital margins and a depressed fracture of the outer wall of the frontal sinus in the midline There were no abnormal neurological signs on examination nor any signs of shock, the pulse rate being 68, respirations 20 per minute, and the blood-pressure 150/80 mm Hg There were no obvious signs of injury to the abdomen or the chest The patient had passed clear urine since the injury

Operation —At 10 A M, next day, under general anæsthesia, the supraorbital wound was cleaned and excised, the fracture involving the orbital margins was reduced, and the wound was closed in layers

Postoperative Course —On his return to the ward the patient became very restless and began to vomit what appeared to be altered blood Later in the day he complained of pain in the epigastrium and breathlessness There was no shoulder pain The pulse rate had increased rapidly to 128 and respirations to 40 per minute, while the blood pressure had dropped to 90/60 mm Hg

On examination, the patient was extremely pale and sweating profusely, with anxious facies, and lying on his right side with his knees flexed The apex beat was 2½ inches from the midline in the fifth left intercostal space The heart sounds were normal The left side of the chest was immobile on respiration and dull on percussion as high as the third left intercostal space anteriorly There was complete absence of breath sounds over this area, and no adventitious sounds were heard There was good air entry in the right lung The abdomen moved normally on respiration, there was tenderness and guarding over the left hypochondrium and epigastrium, percussion revealed a normal area of liver dullness, and bowel sounds were absent Rectal examination revealed no abnormality A provisional diagnosis of ruptured diaphragm with hæmothorax was made, and in view of the rapidly deteriorating condition of the patient immediate operation was considered advisable

Second Operation —The abdomen was explored through a left paramedian incision. There was no free fluid or blood in the peritoneal cavity A large oblique tear, 5 inches long, was felt in the left cupola of the diaphragm The region of the left kidney and splenic flexure of the colon was contused The stomach and spleen had herniated into the left pleural cavity through the tear in the diaphragm A thoracotomy with resection of the left ninth rib was next performed, this rib was found to be fractured in the mid axillary line The stomach was much dilated and thin walled, with numerous subserous hæmorrhages As it could not be reduced through the diaphragmatic tear, its contents were aspirated, three pints of coffee coloured fluid being recovered The stomach and spleen were then returned to the abdominal cavity, and the tear in the diaphragm was sutured with 'Mersilene' The thoracotomy incision was closed with drainage of the left pleural cavity, and the laparotomy incision was closed without drainage Blood (2 pints) was given intravenously during the operation

Recovery was uneventful Daily radiography of the chest showed a completely expanded left lung, with a little effusion of fluid at the left base after the fourth day this effusion gradually resolved A month later a barium meal showed no evidence of intrathoracic herniation, and radiography of the chest revealed complete expansion of the lungs

Comments

This case is of interest because the abdominal contents must have herniated into the thorax after the administration of the first anæsthetic for suturing the supraorbital margin The stomach presented the picture of acute dilatation Most of the published cases of traumatic hernia have developed insidiously, appearing from a few days to many weeks after the original injury Frequently the diaphragmatic lesion had been overshadowed by more serious intrathoracic or intra abdominal complications

We have been unable to find any reference to the enormous gastric dilatation noted in the present case It seems likely that, at the moment of injury, the diaphragm ruptured explosively owing to increased intra-abdominal pressure Later on, during the induction of anæsthesia and possibly associated with straining, the tear became large enough to allow herniation of the stomach and spleen into the thorax, and the constriction at the hernial orifice caused great dilatation of the herniated stomach

This [illegible] illustrates the importance of making a [illegible]ical examination in cases of injury to the head, not only at the time of admission but also dur the ensuing stages of return to consciousness

We are indebted to Mr Norman Whalley for permission publish this report

REFERENCE

Evans C J, Simpson, J A (1950) *Thorax*, 5 343

Preliminary Communication

HYALINE MEMBRANE IN THE LUNGS OF THE NEWBORN

IN recent years much work has been done to elucid the nature, source, and cause of hyaline membrane the lungs of newborn infants Farber and Wilson[1] showed that similar membrane is sometimes formed other conditions, and Farber[2] later demonstrated th œdema and membrane could be produced in rabbits b bilateral mid cervical vagotomy Others[3–6] have a shown that various experimental procedures may prod a similar disease pattern in the lungs of animals, and it generally agreed that a number of agents and proces may lead by one or more mechanisms to a comm histopathological finding

Histochemical analyses of the membranes[3–6] as foun in premature babies and in experimental animals hav established the presence of a polysaccharide aldehy Wagner,[7] who has carried this a stage further, belie that the membrane contains mucoprotein and that it formed from endogenous mucus derived from the na pharynx, buccal cavity, and bronchial tree of the inf Other observers[3] have been unable to demonstrate muc in hyaline membranes by histochemical methods, a this does not surprise us, since we have found that th epithelium of the respiratory bronchioles is muc negative, and that the only mucus secreting gla present are sparse subepithelial acini Very rece Gilmer and Hand[8] concluded from morphological stud that the membranes are endogenous, and, by th application of two methods hitherto not used in the st of this disease, we ourselves have come to the s conclusion Our methods seem to reveal both the nat and source of the membranes

Using frozen sections of formalin-fixed material, applied the Lepehne Pickworth benzidine nitropru peroxide technique[9] By this method the erythroc were stained an intense blue black as expected, but th hyaline membrane took on a uniform rich royal bl colour The occasional blue black red cell could be eas identified as an entirely distinct body in the membra It was further noted that the epithelium of the respirato bronchioles and alveolar ducts showed a rich royal bl granularity, and in some cases this granularity was intense that the epithelial cells were seen as a unifor royal-blue The intensity of this royal blue staining o the membranes and epithelium was somewhat less material which had been in formol saline for 3–5 month

At this stage we realised that we were dealing wi either organic iron or peroxidase enzyme, or both We then found that previous treatment with 5% sodium cyanide, or 5% sodium azide, or steaming for 5 minutes in each case reduced the intensity of the royal blu staining, but did not abolish it However, we noted als that lengthy treatment of frozen sections by these method abolished the staining reactions by removal of the membranes and granules From these observations ar m the fact that the staining intensity was diminished – material which had been fixed for a long time in mol saline, we concluded that the reaction was due rtly to enzyme but mainly to organic iron

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[1] Farber S, Wilson, J L *Arch Path* 1932 14, 437
[2] Farber S *J exp Med* 1937 66 397
[3] Blystad W, Landing B H Smith C A *Pediatrics* 1951 8
[4] Miller H C Behrle F C, Gibson D M *Ibid*, 1951 7 611
[5] Tran Dinh De Anderson G W *Obstet Gynec Surv* 195 8 1
[6] Bruns P D, Shields, L V *Amer J Obstet Gynec* 195 67 1224
[7] Wagner J C *Lancet* 1954 ii 634
[8] Gilmer W S, Hand A M. *Arch Path* 1955, 59, 207
[9] Lillie R D Histopathologic Technic Philadelphia 194 p 119

To test these conclusions we applied the Nadi ction to frozen sections by placing these in 1% alpha phthol (alcoholic) for 5 minutes and then for 5 minutes 1% aqueous dimethyl para phenylene diamine By s technique the hyaline membranes and granules in e respiratory bronchioles were stained a purplish blue the indophenol blue, the staining of the red blood-cells ing more intense but of the same colour Prior treat ent of the sections with cyanide, &c. was found to minish but not abolish the staining reaction

The lungs of several controls were examined by both chniques, and from these it was apparent that the nsity of the specifically staining granules in the spiratory bronchiolar epithelium was inversely pro ortional to the gestation age and that it was greater in ematures dying of hyaline membrane disease than in mparable prematures not having this condition owever, the intensity of the granularity was much less very premature infants (less than 1200 g) Further was apparent that the specific granularity of the ithelia of the respiratory bronchioles and alveolar cts increased with respiration since it was virtually sent in lungs atelectatic from birth and in those of llborn infants The œdema fluid in adult cases of rebral trauma and in cases of bulbar poliomyelitis was nd to contain abundance of these specific granules enly scattered throughout the fluid and it was clearly ident that drying and condensation of such pulmonary dema fluid would lead to formation of a membrane hich would stain uniformly by the techniques used

It is very unlikely that these specific staining reactions the hyaline membranes are due to diffusion of material o the membrane In the first place the staining is o even for a diffusion phenomenon Secondly where uld this material come from except from the respiratory nchioles which we have shown to be laden with nules of the same staining reactions ? Hæmolysis as use is also unlikely, because the reactions were found cases with no pulmonary hæmorrhage and because a case of hæmorrhagic pulmonary disease of the new rn, where hæmolysis was evident in the presence of st red cells the picture was patchy and uneven ally we have found that the two reactions work ilarly and equally well in deep frozen unfixed lung ue from a case of hyaline membrane disease

It seems to us most likely that the common factor ponsible for the two reactions (Lepehne Pickworth d Nadi) is the cellular respiratory enzyme system tochrome-oxidase/cytochrome C It is indeed possible at respiratory enzymes are produced in the granules hich we have demonstrated in the epithelia of the piratory bronchioles and alveolar ducts and it is mpting to suppose that this enzyme system is an tive secretion of the epithelia An analogy may there to be drawn between infants developing hyaline embrane disease and the experimental rabbits of rber in that both probably suffer from an uncontrolled cretion of this enzyme system Further it is very obable that the actual hyaline membrane represents condensed and dried accumulation of this secretion, pecially as it is conceded that the only factor known modify the incidence and severity of this disease is gh humidity

We cannot at this stage be certain that the substance(s) ving rise to the reactions described here are cytochrome-idase/cytochrome-C since other metallic porphyrin otein complexes could be responsible for similar stochemical findings

Department of Pathology
The General Hospital
Sudbury Ontario
Canada

MATTHEW J LYNCH
M.B M.R C.P

LES D MELLOR
F.I.M.L.T S T

Medical Societies

ROYAL SOCIETY OF MEDICINE

Metabolic Factors and the Infectious Process

THE section of pathology met on April 26 under the chairmanship of Prof L P GARROD the president to hear Prof RENÉ DUBOS, of the Rockefeller Institute, New York discuss the Effects of Metabolic Factors on the Infectious Process

Professor Dubos described experiments by which the expectation of life of mice infected with tubercle bacilli and also with strains of staphylococci salmonella, and klebsiella could be shortened. He had found that the expectation decreased when animals were exposed to various stresses" before inoculation A number of different stresses had been used including the administration of thyroxine or dinitrophenol, in such doses as to inhibit the animal's normal weight gain, or of sodium citrate and α keto glutarate The simplest method however, was starvation for thirty-six hours before inoculation and this method had given the most striking results. The results after starvation could not be explained simply by calorie deprivation for low-calorie diets adequately varied in constitution, which reproduced the effects of starvation, did not decrease the animal s resistance moreover the effects were observed too soon and were too quickly cured for this to be likely Nor was it simply weight loss that produced the effect for mice fed on diets so low in protein that their normal weight gain was offset were normally resistant to infection Professor Dubos had also shown that the most effective way of lowering resistance was by starvation for forty eight hours before inoculation and that recovery was complete after forty-eight hours on the standard Sherman diet On the other hand when the mice were fed with a mixture containing adequate fat, carbohydrate minerals, and vitamins but with essential amino acids in place of protein the state of increased-susceptibility was indefinitely prolonged Normal resistance was not restored until a whole protein was added. Not all proteins were equally effective in this respect, and of those tested casein was the best

The results could be explained either by increased susceptibility of the animals to the bacterial toxins or by more rapid and extensive bacterial growth It had been found that, after thirty-six hours of fasting mice were more sensitive to endotoxins from gram negative organisms and to the recently isolated tuberculous toxin so that the LD_{50} was reduced to a half or a third of that for normal animals Starvation for forty-eight hours, followed by a diet low in protein would reduce the LD_{50} to a tenth But these comparatively small effects could not explain the observed change in susceptibility

In other experiments bacteria were injected intravenously in mice and later estimated quantitatively in various organs—with remarkable results Two groups had been studied : one had the standard Sherman diet (group 1) and the other had a diet low in protein and was then starved for forty eight hours (group 2) Both groups were *inoculated* with a dose of 10^6 Friedländer s bacillus (group III) and their organs examined quantitatively for bacteria ten hours later with the following results

	Spleen	*Liver*	*Blood*
Group 1	0 0 18	1 1 0	Sterile
Group 2	12–6000	10–50 000	+ + +

Similar results were obtained with other organisms—e.g staphylococci—and using other forms of stress, such as increased carbohydrate intake or thyroxine administration

Professor Dubos concluded that the effect of malnutrition was to impair the local bactericidal powers of tissues possibly through depression of the reticulo-endothelial system It has been shown (Berry and Mitchell) that if the Krebs cycle was poisoned the animal's resistance was likewise depressed Therefore it seemed that the observed change in susceptibility might be explained by (*a*) lack of cellular glycogen, or (*b*) decreased glycogenolytic activity by the cell, or (*c*) lowered levels of polycarboxylic acid in the tissues All these effects led to impaired clearing-power of the reticulo endothelial system, decreased bactericidal power of the tissues, and decreased resistance to bacterial toxins Impaired antibody formation could not be cited, for mice had no natural immunity to Friedländer's bacillus

Summing up, Professor Dubos made three points (1) susceptibility to infection in mice can change rapidly as a result of various stresses, (2) the effect is rapid in onset, and rapidly reversible, and (3) the factors concerned seem to be independent of those taking part in the host's normal physiological processes

Prof A A **Miles** discussed the vascular phenomena during the earliest stages of infection He had found that the local reaction to the subcutaneous inoculation of organisms could be abolished by adrenaline, and that if this was done survival of the inoculum was enhanced tenfold The effect could be obtained only if adrenaline was injected locally within four hours of the bacterial inoculum Similar results were observed when the complement was inhibited by 'Liquoid' When the experiments were repeated using the vole bacillus, adrenaline was found to have little effect, but liquoid greatly enhanced survival in the local lesions By using histamine or a globulin permeability factor the local lesion was reduced in size to that of one produced by a tenth of the inoculum in untreated animals

Dr D A **Long** spoke on hormone balance in allergy and immunity He emphasised the importance of choosing a laboratory animal which showed similar immune and allergic reactions to man and which responded similarly to hormones, if the results were to be extended to man He described a series of experiments by which he had shown that the guineapig was a suitable animal He went on to show that significant variation in allergic response was obtained with several hormones Anti- and pro-diabetic factors exerted an effect, and significant desensitisation of tissues had been obtained with a recently isolated and quick acting thyroid derivative Sensitivity to tuberculin could be related inversely to blood sugar levels, and partial pancreatectomy prevented the increased response seen after treatment with thyroxine, which therefore acted through the islets of Langerhans He concluded that immunity was probably due to the balance between insulin and cortisone at any one time

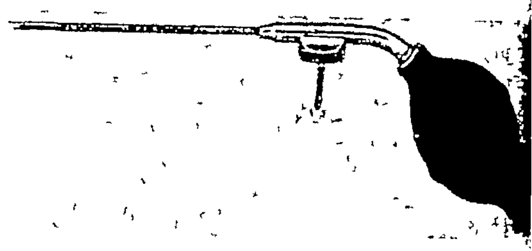
Dr G G **Meynell** discussed the protective function of the gastro intestinal tract against infection He had found that *Salmonella typhimurium* was killed at pH2 in two to three minutes He had also shown that if the gastro intestinal flora in mice were modified by the administration of streptomycin, their resistance to an oral dose of *S typhimurium* was decreased, and also that the organisms given by mouth could be recovered from the large gut This type of effect might be important in man

During the discussion, Dr **Brian Lacey** wondered whether sufficient attention had been paid to the genetic constitution, age, and sex of the mice used, and Dr A Felix, F R S, asked whether Professor Dubos's results were to be explained solely in terms of local cellular effects, or whether antibodies could account for some of them Professor **Dubos** felt that all the observed effects were probably mediated through a common channel, which facilitated both local tissue reactions and antibody res[illegible] On the question of applying the results of [illegible]ments to man, he said that no one knew better than he that mice and men were different, but justified the choice of a different animal when question to be answered by the experiment was sp and sufficiently limited

New Inventions

A MODIFIED THROAT SPRAY

In throat sprays used for spraying the throat befo endotracheal intubation or instrumentation, the b is joined to the nozzle by a flexible tube, with the re that the operator has to use both hands, and may n the services of an assistant The throat spray illustrat



here can be operated single-handed It is simple a sturdy in construction, inexpensive, and effective T nozzle is long enough to be introduced between th vocal cords for local preparation of the trachea. T Macintosh-type container keeps the volume of lo anæsthetic within safe limits and has the addition advantage of being unbreakable With a shorter nozz the spray should also prove valuable in otolaryngology

The instrument can be obtained from Medical & Indus Equipment Ltd, for whose coöperation I am grateful.

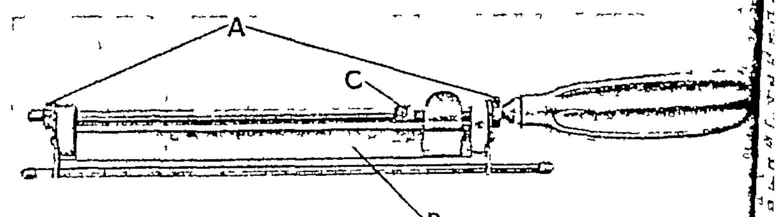
Mark Swerdlow

Manchester M.D, B SC Manc., F.F.A R C.S., D.A

MODIFICATION OF HUMBY KNIFE

There have been several modifications of the orig Humby knife, with the aim of making it lighter enabling the blade to be readily replaced and adju In a new model, made at my suggestion by M Allen & Hanburys, these modifications have b combined, and in this model the instrument need not dismantled to replace the blade Ease of sterilisation storage have also been considered

This new modified Humby knife is light and w balanced Adjustment between the roller and the b from 0 01 mm to 1 0 mm is made by two kn collars (A) mounted on the back of the knife The bl



$6^1/_4$ in long, is of the wafer-razor type and is lock securely in a leaf-spring holder (B) To fit a new bl it is only necessary to move a safety catch (C), open th leaf and insert the blade under the roller, and repla the safety catch

The knife without the blade can be sterilised b boiling, without risk of damage, and the blade sterilis in the same manner as the standard interchangeab scalpel blades Since the blade can be fitted and remov quickly and easily, no protective cover is necessary f sterilisation or storage.

Fenton Braithwait
O.B.E, M.A, M.B Camb.,
M.SC Manc., F.R.C.S
Plastic Surgeon

Royal Victoria Infirmary,
Newcastle upon Tyne

Reviews of Books

roanatomical Basis for Clinical Neurology

TALMAGE L. PEELE, M.D., associate professor of anatomy in charge of neuroanatomy, Duke University School of Medicine New York and London McGraw Hill 1955 Pp 664 100s

UCH has been said of the necessity for integrating siological and anatomical knowledge with sub- ent clinical training Most formal textbooks of tomy do, in fact, include paragraphs, usually in very ll print, devoted to applied anatomy Unhappily h excursions rarely succeed and it is often hard to ern the true links between form function, and deal disorder Dr Peele in this new textbook is very nitely aware of the trefoil nature of this teaching blem and equipped with a practical training in earch neuro-anatomy and clinical neurology, he has acked it *in admirable fashion*

fter a short but adequate and well illustrated account he histological and embryological details of the nervous tem, he gives formal sections on descriptive anatomy of its ious components. In each section however there also ears comment on the physiological factors relating to the ctures described together with some of the more important hological changes to be expected and their clinical mani ations. Thus the account of the blood supply and ven ular system of the brain is followed by a short discussion he circulation of the cerebrospinal fluid a description of its mical and physical properties, and the clinical aspects of reased intracranial pressure Similarly the factual account he spinal cord is accompanied by physiological and clinical ail which though brief will at once inform and stimulate preclinical student In discussing recently acquired tomical knowledge Dr Peele maintains his standards nature and activity of the reticular formation are clearly ribed and recent electrophysiological work on the ebellum is succinctly presented. Some of this more con versial evidence is perhaps offered a mite too firmly but teaching it is important to take up a reasonably definite itude. He is in any case to be congratulated on the healthy ticism he displays about the present evidence on the ppressor zones.

his admirable book is well illustrated and includes omprehensive bibliography

dern Trends in Ophthalmology

3rd series. Editor: ARNOLD SORSBY M.D., F.R.C.S London: Butterworth 1955 Pp 346 65s

rofessor Sorsby is again to be congratulated on his rnational team of contributors, who give an admirable vey of knowledge which has not yet reached the tbooks. The book is arranged in sections dealing in n with the basic sciences on which ophthalmology ts, advances in diagnostic procedures, clinical and perimental pathology clinical aspects in treatment, d social aspects. Adequate space has been given to the est developments in anatomy physiology and patho- y and Professor Sorsby himself has contributed good pters on the nature of malformations, and on strepto- cin and the new antibiotics, as well as on the social pect of blindness. With Miss Mary Savory he also tes on cortisone and corticotrophin in diseases of e eye

actions with Drug Therapy

HARRY L ALEXANDER M D emeritus professor of clinical medicine Washington University medical school Philadelphia and London W B Saunders. 1955 Pp 301 52s 6d

THE increased frequency of drug reactions in the past o decades has prompted Professor Alexander to compile s volume. He defines the reactions as lesions occurring only a small proportion of treated patients, differing om pharmacological effects and overdosage effects of e drugs and induced by therapeutic or subtherapeutic ounts

Only a few reaction patterns occur the main ones are matological manifestations, blood dyscrasias, serum sickness, shock, bronchial asthma, hepatitis, and polyarteritis nodosa. In the opening chapters of the book these patterns are described and their mechanism is discussed Controversial aspects of the subject are not fully discussed and this section is clearly not addressed to the specialist The general clinician may find the argument difficult to follow in places, and in many passages the syntax suggests overhasty revision. In the second part of the book many commonly used drugs and the reactions to which they give rise are described. Here the presentation is clear and informative and a coherent text replaces the catalogue common in works of this kind

Vitamins and Hormones

Advances in Research and Applications Vol XII Editors ROBERT S HARRIS professor of biochemistry of nutrition Massachusetts Institute of Technology Cambridge Mass; G F MARRIAN professor of medical chemistry University of Edinburgh; KENNETH V THIMANN professor of plant physiology Harvard University Cambridge Mass New York and London: Academic Press. 1954 Pp 303 $7.50

THE emphasis in this volume has been on vitamins, and consequently on nutrition; but three of the eight articles deal with hormones.

The first by John Hammond of Cambridge deals with the effects of light on hormone production and is concerned chiefly with seasonal changes, particularly those of reproduction which can be induced in warm blooded animals by modifying the illumination There is an interesting review by R B Bradbury and D E White (Western Australia) on oestrogens and related substances in plants, and one for practical men by F W Lorenz (California) on the effects of these oestrogenic hormones on the domestic fowl and their value in the poultry industry for fattening and other purposes. There are two papers on vitamin A—one by Saul H. Rubin and Elmer De Ritter from the Hoffmann La Roche laboratories, New Jersey dealing with the vitamin A requirements of animals, and the other by C Nieman and H J Klein Obbink of Amsterdam, dealing with the biochemistry and pathology of hypervitaminosis A. Both these papers are pertinent at the present time since the synthesis and large scale production of vitamin A has recently been effected by Hoffmann La Roche The authors give a valuable table summarising the dosages which have already proved toxic for man and the times for which they were administered Two English scientists, S K Kon and J W G Porter have contributed an account of that most complex but important subject the synthesis of vitamins in the ruminant: it now appears certain that the host and the micro-organisms in its rumen have established a nutritional symbiosis which is responsible for the provision of far more than the vitamins which the host requires. The article on the chemistry of vitamin B_{12} by Karl Folkers and Donald E. Wolf who are working in the Merck laboratories New Jersey is the most highly specialised and also the longest paper in the volume. The article by Charles S Davidson of Boston Massachusetts, on disturbances in nutrition relating to liver disease in man is a short and very readable account of current views on kwashiorkor alcoholic cirrhosis and other clinical disturbances in which the liver plays a prominent part

Doctors may be recommended to begin reading here; chemists, physiologists, and animal husbandmen will probably begin somewhere else in the volume but all may be recommended with confidence to begin.

A Handbook of Emergency Toxicology

A Guide for the Identification Diagnosis and Treatment of Poisoning SIDNEY KAYE B.S M SC associate professor of legal medicine Medical College of Virginia Springfield Ill Charles C Thomas Oxford: Blackwell Scientific Publications. 1954 Pp 303 42s

HE is a brave man who sets out to write an acceptable book on toxicology for the subject matter is about as inspiring as the contents of Bradshaw or a street directory Mr Kaye's great diligence shines out from the pages of his handbook but he has been no more successful than his predecessors in writing a best-seller

Upwards of 200 pages are occupied by a routine review of common poisons arranged alphabetically A telegraphic style is adopted this may be an advantage in a book designed for quick reference, but it inevitably makes this part of the text unreadable There is a table showing the names of the poisonous constituents of a large number of proprietary compounds —headache powders, weed killers, and the like Another table sets out the poisons contained in household articles—cosmetics, inks, matches, metal polish, and a score of the other perils that lie about us in our infancy It is difficult to imagine that anybody will get much help from the chapter on symptoms and signs to list 29 poisons and 15 diseases which may cause vomiting, purging, and abdominal pain does not suggest a very enlightened approach to toxicology, a few general principles would have been more valuable, especially if the subject could be correlated with physiology, pharmacology, and clinical medicine The author devotes only a paragraph to general considerations in this chapter, and the guidance here falls short A chapter on analysis provides a short survey of some of the chemical techniques of toxicology, but it is too meagre to interest the analytical chemist or the hospital biochemist In a book for students and practitioners, a competent essay on the collection of samples for expert analysis would be more valuable

Such books as this provide the best of all arguments for transferring the teaching of toxicology to departments of pharmacology, where the basic sciences are steadily ousting empiricism

Modern Trends in Psychosomatic Medicine

Editor DESMOND O'NEILL London Butterworth 1955 Pp 375 55*s*

PSYCHOSOMATIC medicine, though new in some of its aspects, is as old as medicine itself in others Some of the twenty articles in this fourteenth volume of the excellent *Modern Trends* series set out old and well-accepted views on the influence of the mind on the body, others offer less well-known and certainly less well-accepted ideas on a diversity of bodily, emotional, and psychiatric conditions The book contains most of the clinical evidence relating such disorders as thyrotoxicosis, ulcerative colitis, asthma, and skin diseases to psychological disturbances, and reviews the psychosomatic concept in medicine in general To the enthusiast it will offer a multitude of opinions confirming his belief that almost every illness is due to psychological stress In the sceptic it may provoke bewilderment and doubt that so much can be attributed with such confidence to such a cause, for though parts show a true and keenly scientific approach and parts are statistical, other chapters are mainly conjectural, and a few are almost frivolous The pleasantly classical and humanistic flavour of much of the writing is refreshing, and the references are copious and well chosen Dr O'Neill is to be congratulated on presenting such a full and varied picture of his subject, even if it may seem, perhaps inevitably, more one-sided than it should

Diagnostic Advances in Gastrointestinal Roentgenology

Selected Methods, with Clinical Evaluation ARTHUR J BENDICK, M D, director of radiology, Beth Israel Hospital, New York New York and London Grune & Stratton 1954 Pp 131 $6 00

IN the preface to this book the author states that "it is not intended for beginners but for radiologists of several years' experience, so situated that they cannot keep up with all the new techniques or the more modern interpretations of roentgen findings" Unfortunately it fails of this purpose, for it contains many inaccurate statements

Thus we are told that gravity does not play any appreciable part in the passage of barium from the œsophagus to the stomach, that the detection of neurological interference with swallowing is aided by demonstrating less distinct elevation of the hyoid bone on the films (but not how or under what circumstances), that the "club soda" technique in achalasia can be used as a method of deciding operability (but not how), and that amyl nitrate (not nitrite) is given to demonstrate the cardio œsophageal junction in achalasia We are told too "that the muscle of the diaphragm plays only a minor role in constricting the œsophagus at its lower end"

It [illegible] not, on the whole, to be able to recommend a b[illegible] ich a sound object

Antenatal and Postnatal Care (8th ed Lond J & A. Churchill 1955 Pp 672 37*s* 6*d*) —In p this edition of his reliable and senior textbook Prof F. Browne has had the collaboration of his son, Prof. J McClure Browne This family combination seems to worked well In including new work on the toxæmias pregnancy they draw attention to the work at the Wome Hospital, Sydney, Australia, where a determined campa to prevent eclampsia has resulted in a decline in incide from 1 in 400 in booked patients in 1946 and 1 to 1 in 20,000 patients since, in the 1 failure, a ri blood-pressure had been overlooked The Brownes find t in every eclampsia patient there are one or more warn signs which should lead at once to prophylactic treatment, their book does everything possible to ensure that th and other warning signs, in pregnancy and after, are missed

Alexander the Great and his Time (London Rock 1955 Pp 300 25*s*) —Dr Agnes Savill, well known as th editor of her husband's popular *System of Clinical Medic* has turned historian and here recounts the adventurous romantic story of Alexander the Great Alexander beca king of Macedon on the murder of his father, inheriting best equipped and trained army in the world At the age twenty he made himself master of Greece and began wonderful conquests marching from Macedon across th Hellespont to Egypt and from there through Persia to th upper reaches of the Indus in Hindu Kush When he d at the age of thirty three he had marched with his ar nearly twenty two thousand miles often under unbeliev difficult conditions He fought innumerable battles, us after a long forced march or a hurried climb up what enemy believed to be an unclimbable cliff or mount His weapons were surprise, swiftness of decision, imaginat foresight, ability to inspire and maintain the coöperat of his subordinates, and superb physical fitness and athl skill Dr Savill has written an interesting book. On left wondering whether she does not rebut too freely of the calumnies heaped on Alexander by some histori But if she tends to gild her lily, she leaves no doubt the reader's mind of the qualities that made Alexa great

Principles of Internal Medicine (2nd ed Lond H. K Lewis 1954 Pp 1790 £5 10*s*) —When the edition of this book by Dr T R Harrison and his coll was published in 1950, it was at once accepted as an auth tive textbook of American opinion The second e establishes it even more firmly as a standard work of ref The general arrangement is the same as before The third deals with general considerations and the rem considers the different systems of the body one by A new chapter on the general care of the patient gi useful review of nursing principles and the treatment symptoms in general The new edition is some 200 p longer than its predecessor, and with somewhat c print and some compression of space it contains a great more—Chapter headings have gone and some of the illus tions have been much reduced in size The index has, great gain, been almost doubled in size The contribu now number 85, an advance of about 30 An important section of over 100 pages, which replaces the section weakness, is written by Dr R D Adams and his asso and includes an excellent and lucid account of the an states, depression, sleep disorders, fits, delirium, co and the psychoses

I was a Drug Addict (London Rider 1954 Pp 15*s*) —Although Mr Leroy Street assures us that his acc is "uncoloured" the literary form evidently owes much to collaborator, Mr David Loth, who is a professional wr Fewer sentences such as "these homely objects were abo convey a new meaning to my specially alerted brain," fewer verbatim conversations would make the auto graphical statement seem more authentic As it sta however, it describes, in rather exaggerated language subjective experiences and the companionship which drug addict meets in his descent There is no obvi improbability in all this, except for the happy ending wh represents permanent recovery as the outcome of a fortu self directed plan for reducing the dose of morphine grad The work has social rather than medical or psycholo interest

THE LANCET

LONDON SATURDAY MAY 14 1955

Orbital Leucotomy

Standard leucotomy, or lobotomy developed y **Freeman** and **Watts** in which a large part of the refrontal areas is severed from the rest of the brain, as of late been carried out only in cases of long anding mental illness with severe behaviour dis rder Apart from the unpredictability of its atomical results it commonly causes undesirable rsonality changes These changes, it was observed, ere more likely to occur when the operation had een extensive and attempts were therefore made to mit it to a minimum Clinical observation of atients with frontal lobe injuries, as well as experi ental work, suggested that a regional factor was portant Several workers reported satisfactory sults from "lower quadrant" operations aimed at olating only the orbital part of the frontal lobes hese, like the standard leucotomy, were still blind rocedures lacking in precision With the increasing e of open operations various selective methods have een developed. One of the most interesting of these the undercutting of certain parts of the frontal rtex first proposed by **Scoville**[1] who compared e effects of undercutting three cortical areas with ose of standard leucotomy The areas chosen were e superior surface of the frontal pole the orbital urface, and the medial surface of the cingulate gyrus e found that in schizophrenia and the affective tates undercutting the superior or the orbital surface rought about the same results as the standard peration, but with less personality defect. He garded undercutting of the orbital surface "as e ideal operation for psychoneuroses and the milder ood disturbances because of the almost complete bsence of personality changes There was much o recommend the choice of that particular area for atients with otherwise intractable anxiety and epression

The importance of this area as part of the cerebral ubstrate of emotional integration is now generally ecognised **Tow** and **Lewin**[2] described the results f undercutting the orbital surface in twenty patients ith various mental disorders who were subsequently followed up for two years. The effects were comparable with those of the standard operation, but the personality changes were less pronounced. Two reports on earlier pages of this issue appear to confirm the value of the method Dr **Ström Olsen** and Mr **Northfield** have applied it to a group of patients with chronic neurotic tension states, in each of these patients, including one with pronounced paranoid ideas, depression was prominent More than half recovered from their symptoms and personality changes were slight Another group, suffering from long standing schizophrenia with personality deterioration, did less well Mr **Knight** and Dr **Tredgold** report on a series of fifty two patients subjected to a slight modification of cortical under cutting Their results are almost as impressive as those of **Ström Olsen** and **Northfield** They also found that improvement was most striking in patients with anxiety and depression Patients with hysterical symptoms did not respond favourably The two reports confirm the beneficial effect of orbital under cutting and the absence of severe postoperative personality changes, but it is difficult to compare the results in detail since these were differently assessed. **Knight** and **Tredgold** eschew the term "recovered" used by the other group of workers, but it can be assumed that the majority, if not all, of their "much improved" patients would have been classed among the "recovered" by **Ström Olsen** and **Northfield** Evaluation and classification of therapeutic results is a serious problem in psychiatry, and communication between workers in the same field is often bedevilled by the pitfalls of semantics

The fact that an operation as limited as orbital undercutting can produce a substantial and often dramatic change in the mental state seems at first to contradict the view held by earlier workers that the degree of improvement depends chiefly on the amount of brain substance isolated **Meyer** and **Beck**[3] suggest that, though the extent of the operation is important regional localisation of the cut within the frontal lobe also influences the effects They point out that some very limited regional cuts may in fact, by severing the thalamofrontal projection, isolate large areas of cortex The question, therefore whether the frontal lobe functions by mosaic or mass action has still not been finally answered In their experience, the extent of the cut, wherever localised is correlated with improvement But various types of improvement follow surgical interference with frontal lobe function one is the complete disappearance of symptoms, especially of depression, immediately after the operation almost any operation on the frontal lobe however limited has sometimes resulted in this dramatic change In such instances at any rate, improvement or even recovery does not seem to have been bought at the price of a severe personality change, so obvious in other patients The results of cortical undercutting show that notoriously reversible symptoms, such as depression and anxiety, can be removed sometimes by a very limited operation—an effect which, though profound, is clearly unrelated to the personality change

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[1] Scoville W B J *Neurosurg* 1949 6 65 *Proc R Soc Med* 1949, 42, suppl 1 3

[2] Tow P M, Lewin, W *Lancet* 1953 ii 644

[3] Meyer A, Beck E Prefrontal Leucotomy and Related Operation Edinburgh, 1954

In what type of patient can one expect such a distinct improvement? Here we are still in the dark Ström-Olsen and Northfield consider that neuropathology may some day provide the answer Some workers believe that it will eventually be possible to produce lesions to suit every condition and every patient The fact that the results of a precise and limited operation, such as orbital undercutting, are still inconstant, suggests that the effect does not depend only on the extent and localisation of the lesion The patients' personality—the sum total of his response patterns, innate and acquired—must be of considerable importance Only when we know more about the reactions of the personality to sudden alterations in the emotional charges shall we be able to predict the effects of surgical treatment in individual cases The psychiatrists, it is true, have been aware of this, and have generally accepted that in well-integrated personalities the likelihood of undesirable postoperative behaviour features, even after extensive operations, is small, but beyond this we know very little Naturally, clinicians are more interested in their successes, especially when a method has still to be established But the time comes when careful and systematic study of failures and partial failures is at least as important as that of successes This is particularly true in the present stage of the surgical treatment of mental disorders Such studies would also act as a wholesome corrective to the danger of a reversal to "atomistic" concepts of cerebral function The effects of localised operations on mental states have contributed to a revival of concepts reminiscent of those so persistently criticised by Hughlings Jackson, and a language has crept back into medical writings which not so long ago seemed almost extinct What would Jackson have thought of the "intellectual pathways" referred to by Knight and Tredgold? The passage from Le Gros Clark cited by these workers, and Meyer and Beck's[3] recent warning against too atomistic an interpretation of the effects of brain operations, show that at least some of those most familiar with cerebral structure and functions are opposed to a return to the old-fashioned rigid localisation of functions Only by taking into consideration the undamaged parts of the brain and the reactions of the whole personality shall we reach a fuller understanding of the scope and limitations of the surgical treatment of mental disorders

Estimation of Blood-loss

The most important cause of shock after surgical or accidental injury is loss of blood into and from the damaged tissues, or of plasma in cases of burns and scalds, or of crushing Such shock usually responds to the rapid replacement of the lost fluid, but measurement of the amount lost, even at operation, is not easy

Estimates based on impressions during the operation are usually too low, even when reinforced by collection of the swabs, towels, and gowns Surgeons who have not submitted themselves to the discipline of direct measurement of blood-loss usually find it hard to believe the figures obtained in this way Som [illegible] for example, when the operation is for e [illegible] arance of viscera in the pelvis or of a large block of organs in the upper abdomen—estimates based on impressions are of hardly any value, and when, in addition, the operation lasts many hours and is accompanied by transfusion to replace lost blood, direct measurement is especially necessary To be useful the method of direct measurement must provide an accurate answer shortly after the operation has ended Probably the simplest way is to wash out all the swabs, towels, gowns, and instruments in a known volume of water, to which is added the contents of the suction bottle The hæmoglobin level of this fluid is then measured either directly[1] or after conversion to acid hæmatin[2 3] This, together with the hæmoglobin level of the patient's blood before and immediately after operation, gives a fairly accurate guide to the volume of blood lost. Paquin et al[4] have devised a method suitable for cases in which blood or other intravenous fluids are being administered The difference between preoperative and postoperative weight is corrected on the one hand for additions (including dressings and transfused blood or other fluids), and on the other hand for depletion by bleedings, estimated insensible water-loss, resected tissue, and excreted urine and other lost body-fluids As a check they also measure blood-loss directly,[5] by weighing the towels, swabs gowns, and suction-fluid They have found close agreement between the results by these two methods, even for operations lasting ten hours with a blood loss of over 4 litres But they point out that serious errors may arise from the accumulation of shed blood in "dead spaces"—for example, the pelvis—and from excretion of urine or, in operations on the urinary tract, from contamination of blood with urine Furthermore the method of Paquin et al cannot be expected to give really reliable results until we know more about the possibly wide variation in insensible water-loss during different types of anæsthesia and they themselves emphasise that their method should be combined with clinical examination before deciding on treatment Fortunately operations lasting for more than three hours are rare, and the amount of blood lost at operation seldom exceeds 2 litres

Measurement of blood or plasma lost by accidental injury is even less easy Theoretically such loss would be best measured by estimating the amount of blood remaining in the circulation and subtracting this from the normal volume, which, as Gibson and Evans[6] showed, is closely related to body weight But this approach is so studded with pitfalls that others have been tried Noble and Gregersen[7] found that in civilian injuries blood loss depended largely on the extent of muscle damage and the number of fractures, and Grant and Reeve[8] showed that in limb injuries the volume of damaged tissue was a good guide to the volume of blood lost Mr Ruscoe Clarke and his colleagues[9] have

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1 Oppenheim A Pack G T Abels J C Rhoads C P *Ann Surg* 1944 119 865
2 Gatch W D Little W D *J Amer med Ass* 1924 83, 1075.
3 White M L Buxton R W *J thorac Surg* 1942 12 108
4 Paquin A J, Marshall, V F Nathanson B *Ann Surg* 1955, 141 53
5 Wangensteen O W *Minnesota Med* 1942 25, 783
6 Gibson J G jun, Evans W A jun *J clin Invest* 19 16 317
7 Noble R P Gregersen M I *Ibid* 1946, 25 158 172
8 Grant R T, Reeve, E B *Spec Rep Ser med Res Coun Lond* 1951 no 277
9 Clarke R. Topley E, Flear G G T *Lancet*, March 26 19 p 629

easured the increase in the volume of injured limbs d also the red blood cell volume, and have tablished that estimates of blood loss based on ese two measurements agree closely Their findings nfirm the close relation of blood loss to muscle jury, which is particularly severe in fractures volving the shaft of the femur or the pelvis. Never eless, although the bleeding associated with such juries is commonly underestimated, there is still sufficient evidence to justify the very large trans sions of blood recommended by PRENTICE et al[10] arly surgical treatment should be combined with pid transfusion of enough blood to maintain the ood pressure within normal limits The anæmia hich follows severe injury presumably reflects e general post traumatic protein katabolism, and ould not be treated prophylactically by the dministration of blood in excess of that needed to store circulatory efficiency

The Mystery of Dental Caries

DECAYED teeth have caused the human race suffering nd unhappiness for several thousand years In ncient times dental caries was associated with the dea of worms in or around the teeth, and this notion ersists in the primitive cultures of today It seems hat a certain JAQUES HOULLIER (1498–1562) first ast doubt on the existence of dental worms, but that lid not prevent GOTTFRIED SCHULZ, who lived at bout the same period from declaring that the pplication of gastric juice from a pig would expel worms—some even as large as an earthworm—from a decayed tooth[11] GALEN believed that dental caries was produced by an abnormal condition of the blood which affected the internal structure of the tooth and recent work gives some support to this hypothesis The suggestion that micro-organisms might be responsible for caries was first put forward by LEBER and ROTTENSTEIN in 1867[12] A few years later, MILLER,[13] working in KOCH's laboratory in Berlin found that micro-organisms obtained from carious dentine produced lactic acid when cultured in the presence of sugar or starch, and he formulated the chemicoparasitic theory of dental caries In 1925 BUNTING and PALMERLEE identified the commonest acid producing organism in the mouth as *Lactobacillus acidophilus*

The chemicoparasitic theory together with the belief that dental caries is associated with the consumption of small molecule carbohydrates that are readily fermented, has been widely accepted for some fifty years. There is now much evidence supporting the theory, including the increased incidence of caries among Eskimos when refined carbohydrate foods were added to their normal diet[14] Investigations during and after the wars of 1914–18 and 1939–45 also seemed to suggest that when sugar was rationed and other highly refined carbohydrates were scarce the incidence of dental decay in children dropped sharply whereas it rose again sharply in the post-war years. More recently many research workers have come to believe that the incidence of caries is influenced by other factors—the structure of the tooth, conditions affecting the metabolism of the body and the ingestion of fluorides in drinking water Some workers now believe that caries is initiated by proteolysis of the organic constituents of the enamel and that decalcification is secondary

A report just issued by the Medical Research Council[15] throws considerable doubt on the idea that caries in children is caused at least partly by excess of sugar in the diet This report describes trials in London, Liverpool, and Sheffield on the effects of adding extra sugar to the diet of children in residential homes The incidence and spread of dental decay in groups of children aged 2–14 years, was first observed for a year, during which the children received their normal diet containing liberal amounts of milk fresh fruit, and vegetables, and, in most cases supplements of cod liver oil and orange juice The children were then divided into two groups one continued to receive the normal diet while the other received additional white sugar The dental condition of this group was compared with that of the controls at the end of 1 $1^1/_2$, and 2 years Since work by OSBORN et al[16] had suggested that unrefined sugar might contain some factor which tended to protect the teeth from attack by caries, raw sugar was included in the diets of some of the test children. The diets were arranged so that the control groups received 11 oz of sugar a week, while the test groups received just over 22 oz of white sugar or about $21^1/_2$ oz of raw sugar The results were somewhat unexpected Despite the relatively large differences between the amounts of sugar given to the control and to the test groups there was no significant difference in the incidence or the spread of dental caries during the 2 years There were some anomalous findings—for instance, some of the children who received extra white sugar actually had a significantly smaller incidence of caries than the controls—but these findings showed no consistency when the results were surveyed as a whole There was no evidence that sugar affects the two dentitions differently As far as could be ascertained, unrefined sugar does not contain a caries inhibiting factor

None of the children in the trial groups received more than about 4 oz of sweets a week and the report does not prove or even suggest that unlimited sweets are harmless Mr E B DOWSETT, in his presidential address to the British Dental Association in 1951, suggested that sweet-eating by children should be controlled[17] In his view sweets made from glucose—as many now are—are more dangerous to the teeth than those made from sucrose The problem of caries is undoubtedly in the broadest sense dietetic But what aspect of the diet is at fault? Is there a local and external effect on the tooth, or is it systemic and internal? These possibilities are not mutually exclusive and if the latest report has done no more than eliminate another hypothesis that at least brings us one stage nearer the solution

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[10] Prentice T C., Olney J M, jun., Artz C P Howard J M *Surg Gynec Obstet* 1951 99 542.

[11] Guerini, V A History of Dentistry Philadelphia, 1909

[12] Leber T Rottenstein J B Dental Caries and its Cause Translated by Chandler T Philadelphia 1883

[13] Miller W D Micro-organisms of the Human Mouth Philadelphia 1890

[14] Price W A Nutrition and Physical Degeneration California 1945 Waugh, L. M., Donald, B *Amer J Dis. Child* 1911 39 483.

[15] King J D Mellanby M. Stones H H., Green H N The Effect of Sugar Supplements on Dental Caries in Children *Spec Rep. Ser med Res Coun Lond* no 288 H.M Stationery Office 1955 Pp 55 4s

[16] Osborn, T W B Noriskin J N Staz J *J dent Res* 1937 16, 165

[17] See *Lancet* 1951 ii, 71

Annotations

REGULATION OF CARDIAC PERFORMANCE

Starling's classical work on the isolated dog heart demonstrated that the strength of its contraction, and therefore stroke output, was determined by diastolic ventricular volume This accorded with expectation, since the strength of contraction of striated muscle is, within physiological limits, determined by the initial length of its fibres In recent years Starling's law has been much discussed in relation to adaptation of the heart to disease, and an exceptionally well documented symposium on this important topic has now been published [1–9]

Three different sets of observations must be considered (1) on the isolated heart preparation where reflex, nervous, and hormonal influences are excluded, (2) on healthy intact mammals, and (3) on patients with heart disease

In the isolated heart the validity of the Starling principle is accepted,[5] but its exact mechanism is still disputed [6] "Venous return" is often said to determine cardiac output, but in any balanced state of the circulation venous return must be the same as the cardiac output Increased diastolic filling of the heart is much more likely to result from increased venous pressure, and this can occur physiologically by contraction of the spongework of venules and other small peripheral vessels pushing more blood towards the centre Guyton [3] has elaborated the conception of "mean circulatory filling pressure," which is the external squeeze of vessels on their blood content with flow factors eliminated This can be measured experimentally during induced temporary ventricular fibrillation, after which rhythmic cardiac contractions are re started by electric shocks As might be imagined, this "static" filling pressure rises with increasing volumes of blood in the circulation Though most of Starling's data showed a correlation between venous filling pressure and cardiac output, Starling himself appreciated that the filling of the heart might sometimes be greatly increased by very small pressure changes Katz,[10] using Wiggers's methods of accurate optical recording, showed that changes in cardiac output paralleled end-diastolic ventricular pressure It is, of course, better to estimate cardiac performance as *work* rather than simply as *output* Sarnoff,[2] who has re-studied the whole matter, has shown a linear correlation between venous filling pressure and *right* ventricular work, and when the left ventricle was loaded by increasing aortic resistance, pressure rose in parallel in the *left* atrium but not in the right Homolateral correlation is thus of the greatest importance For any given filling pressure the work of individual hearts could be increased by adrenaline or decreased by experimental restriction of coronary flow [2]

In intact animals and man the situation is more complex, since the heart is innervated and is exposed to varying amounts of endogenous adrenaline and other influences which may counteract the influence of changes in venous filling pressure End-diastolic volume and pressure may not always correspond if muscle tone can alter [1] While McMichael and Sharpey-Schafer [11] showed a significant general correlation between cardiac output and venous filling pressure in man, Warren et al [12] emphasised the exceptions to this rule Gregg et al [4] have found in the whole dog a general correlation between cardiac output and filling pressure when raised by intravenous infusion, but the correlation was not clear at lower rates of infusion Gauer [7] demonstrated close correlation between diminishing heart volume and stroke output in monkeys subjected to centrifugation Hamilton [9] reminds us that in many experiments with isolated animal hearts the outputs are artificially set much lower than the expected normal for the particular animal Starling's law might be particularly easy to demonstrate under these conditions Richards [8] calls attention to the Swedish radiographic studies of heart volume, which show clearly that in exercise the heart increases in size only very slightly The increased output of effort is certainly brought about by increased rate and increased emptying of the ventricles—increased emptying has been of special interest since it was realised that under resting conditions the ventricles almost certainly do not empty completely and contain some residual blood at the end of systole

In patients with heart failure due to intrinsic heart disease the output tends to be relatively fixed, dropping to subnormal levels in the more advanced stages Heart rate in failure also tends to settle round 100 a minute Such hearts seem, like the kidney in advanced nephritis, to have lost their flexibility of response With this loss of fine adjustment, Starling's law may be the last resource of adaptation to pathological conditions In failing hearts the common absence of increase in cardiac output during exercise, despite a rising venous filling pressure, and other observations led McMichael and Sharpey Schafer [13] to the hypothesis that the failing heart behaves as though it were no longer responding normally to increases in venous pressure, such increases could even be accompanied by a falling cardiac output, and, conversely, lowering of venous pressure by venesection could be followed by improvement in cardiac output These observations may have to be considered in a new light, for Sarnoff [2] has pointed out that decreasing stroke work at high filling pressure is attributable to regurgitation through the atrioventricular valves The studies of Korner and Shillingford [14] show that some tricuspid incompetence is often present in heart failure The extent of this incompetence and its part in producing the congestive features of heart failure have not yet been fully appreciated

POLIOMYELITIS REVIEWED

WITHOUT doubt the great advances in our knowledge of poliomyelitis in the last few years began with the discovery by Enders, Weller, and Robbins [15] in 1949 that poliomyelitis viruses could readily be grown in tissue-cultures—a discovery which won them the Nobel prize in physiology and medicine for 1954 Thereafter our knowledge of epidemiology, pathogenesis, and prevention expanded at a great rate, and the new ground explored has lately been reviewed in a World Health Organisation monograph [16] In this Enders himself gives a beautifully clear exposition of tissue-culture techniques as applied to poliomyelitis, and Rhodes, Wood, and Duncan illustrate the application of these techniques in laboratory diagnosis Gard writes about the virus itself—*Poliovirus hominis* and the related *P muris* to use the correct terminology The new tissue-culture techniques have been applied first to urgent practical problems, and most of our theoretical knowledge of the virus is still based on earlier studies of infected nervous tissue, in which the virus may represent only one

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1 Katz L N *Physiol Rev* 1955 35 91
2 Sarnoff S J *Ibid* p 107
3 Guyton A C *Ibid* p 123
4 Gregg D E, Sabiston D C, Theilen E O *Ibid* p 130
5 Lorber, V *Ibid*, p 137
6 Rushmer, R F *Ibid* p 138
7 Gauer, O H *Ibid* p 143
8 Richards D W *Ibid* p 156
9 Hamilton W F *Ibid*, p 161
10 Katz L N *Amer J Physiol* 1928, 87, 348
11 McMichael, J Sharpey-Schafer E P *Brit Heart J* 1944, 6, 33
12 Warren J V, Brannon E S, Stead E A., Merrill, A J *J [illegible]* 1945 24 337
13 McMichael J Sharpey Schafer, E P *Quart J Med* 1944 37 123
14 Korner, P Shillingford, J *Brit Heart J* 1954, 16 447
15 Enders, J F Weller T H, Robbins, F C *Science* 1949 109 85
16 Poliomyelitis World Health Organisation Monograph Ser no 26 Geneva, 1955 pp 400 40s Obtainable from H.M. Stationery Office, P O Box 569 London S E 1

millionth to ten millionths of 1% of the tissue It is therefore important to re-examine the properties of the virus grown in the more satisfactory milieu of tissue culture now available; to take only *one point it is* vital for vaccine production to know the resistance of the virus to different forms of inactivation Methods of inactivating virus on the skin are scarcely of less interest, since there is still a possibility that virus on the skin may be implanted by injections and on this matter Bard says "It can only be stated that, as a means of removing or inactivating virus on the skin the use of soap detergents, ether ether alcohol, or chloramine is nothing but a symbolic ritual only iodine might be expected to serve the purpose

Hammon describes the first stage in the striking progress in protection—passive immunisation with gamma-globulin The first large-scale trials in 1951 and 1952 showed that gamma globulin gave some temporary protection against paralytic poliomyelitis, and later work has demonstrated that the all important subclinical infections were not prevented. But mass administration of gamma globulin during epidemics has been disappointing and its use *for prophylaxis of contacts* cannot now be recommended for the first detected case in a family is seldom the first to be infected Hammon suggests that gamma globulin may be most useful in dealing with outbreaks of poliomyelitis in summer camps and boarding-schools. It is clear however that active immunisation is the main hope in preventing poliomyelitis, and in the monograph this subject falls to Sabin and Koprowski Sabin discusses immunity as a result of natural infection of man or experimental infection of animals with special reference to vaccination, and he is much concerned with variations in virus virulence Tissue-culture methods allow the detection of naturally occurring viruses of low virulence, and Sabin's important laboratory experiments have segregated avirulent virus variants which might later be used to immunise man. As we pointed out in a leading article last month[17] both Sabin and Koprowski believe that live avirulent poliomyelitis virus will prove best in the end; and this view may well find wider support when the difficulties that are now besetting the immunisation programme in the United States have been fully investigated Sabin and Koprowski have made considerable advances both in *preparing* avirulent variants *from all three* antigenic varieties of virus and in testing some of them in man There are many difficulties ahead in this field, but there is no reason to believe that they cannot be overcome in the next few years On p 1018 we report some of Sabin's latest findings which he described to a meeting of the Association of American Physicians last week

Our outlook on the epidemiology of poliomyelitis has also undergone some sharp changes of late, and these are discussed in the monograph by Paul Gear and Froeche and *Nielsen* Poliomyelitis is world wide and in nearly all countries paralytic cases have become commoner and the disease has attacked older people The virus has spread widely however *in underdeveloped countries* where the disease has the characteristics of infantile paralysis —that is paralytic cases are less common in adults and are largely confined to infants widespread subclinical infections in infancy protecting against paralytic disease in adult life Similarly the first recorded epidemics in Scandinavia North America Australia and New Zealand fifty to seventy years ago were all infantile paralysis. The sparing of adults suggests that they were protected by previous subclinical infection and it need not be assumed that this was a new disease The changed characteristics of poliomyelitis have in fact been created by our changed hygienic habits Poliomyelitis is today under pressure to spread from underdeveloped areas into a *susceptible* population and if the inter-epidemic period is *long* the risk *of a severe epidemic increases* annually One of the most graphic examples of this is the Hudson Bay epidemic in 1948–49 when 60% of the Eskimoes had paralytic disease, all age-groups were involved the lowest clinical attack rate being in the infants Gear mentions another fact which brings home the changing pattern of poliomyelitis in Nyasaland and Southern Rhodesia paralytic poliomyelitis is today one of the most serious hazards facing newly arrived adult European settlers. Discussing public health measures, Payne points to the anomaly that so far as poliomyelitis is concerned hygienic measures may have done more harm than good He suggests that early in an outbreak, or with inter-epidemic cases, the application of hygienic measures may prevent an epidemic from starting once it has started the large number of sublinical infections makes further steps of this kind valueless

PANCREATITIS

MODERN treatment has greatly changed the clinical course of acute pancreatitis as Kirby et al.[1] have shown by comparing cases admitted to the Hospital of the *University of Pennsylvania* before 1946 with those admitted in subsequent years Of 80 patients in the twenty five years up to 1946 23 (29%) died the majority from vascular collapse shortly after the illness began in 1946–53 110 patients were treated with 21 deaths (19%) Deaths in this second group took place later only 3 (14%) of the 21 deaths took place in the first week of the illness compared with 20 (90%) of the 23 in the earlier group The manner of death has also apparently changed Secondary hæmorrhage which was not observed before 1946 accounted for 11 deaths in the second group, and in this group of those patients with hæmorrhagic pancreatitis who survived about a quarter bled either *from an abdominal* wound or into the alimentary tract Possibly antibiotic therapy has reduced the early toxic effects due to infection, so patients survive long enough for the erosive pancreatic enzymes to damage vessel walls and thus precipitate secondary hæmorrhage; Kirby et al. suggest that this complication may be prevented by proper drainage to encourage the escape of the enzymes.

The most severe form of acute pancreatitis was found after operations involving the pancreas There were 14 such cases with 8 deaths 7 from hæmorrhage In 6 of these 14 cases the pancreatitis followed subtotal gastrectomy in 5 subtotal pancreatectomy in 2 simple biopsy associated with cholecystectomy *and in 1 colectomy for a* growth adherent to the pancreas Obstruction of the pancreatic ducts is known to be a potent factor in precipitating pancreatitis[2] which for this reason is sometimes found in conjunction with carcinoma It is therefore not difficult to understand why pancreatitis follows operations such as gastrectomy or pancreatectomy, that may cause trauma to the pancreatic ducts But this does not explain all cases Millbourn[3] has drawn attention to the possibility of interference with the *blood supply to the pancreas by damage* to the superior and inferior pancreatico duodenal arteries *but* Warren[4] points out that the blood-supply is so generous that ligation of one artery alone would be unlikely to cause trouble Pancreatitis has *arisen as a late* complication of partial gastrectomy, through stagnation in the afferent loop and suggested causes include spasm of the sphincter of Oddi and 'sludging' of pancreatic secretions within the ducts as a result of *medication* and dehydration[5]

Injury to the ducts is the most important cause of *postoperative pancreatitis not only because* it is probably the commonest but also because it should be treatable—if not avoidable In Warren's[4] 7 cases of pancreatitis following partial or total gastric resection, 6 of the patients died with pancreatic necrosis In 4 of these a penetrating duodenal ulcer was reported, in any of these 4 cases a duct may have been damaged, while in a 5th carcinoma of the stomach may have involved the pancreas The pancreatic duct, the accessory pancreatic duct, or both, were damaged at operation for duodenal ulcer on 6 other patients, 3 were spared pancreatic obstruction by the development of a fistula, which healed subsequently or was successfully implanted into the intestine, and in 3 the ducts were reimplanted at the outset, all survived and pancreatitis did not ensue It is not easy to observe either of these ducts lying in inflammatory tissue near the base of a duodenal ulcer, owing to their smallness it is still less easy to reimplant them when they are seen, unless they have been dilated by long continued obstruction In this form of obstruction there may be a place for Duval's[6] ingenious technique for curing chronic relapsing pancreatitis[7] This condition is commonly thought to be due to obstruction at the sphincter of Oddi inducing biliary reflux into pancreas, but Duval doubts this and, believing that pancreatitis is caused solely by the obstruction and that biliary reflux is immaterial, he suggests that the pancreas be drained through its tail by transecting and implanting this into the open end of a Roux-en-Y jejunal loop He has successfully treated 2 patients in this way

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[17] *Lancet* April 23 1955 p. 851

[1] Kirby C. K Howard J M Rhoads J E. *Surg Gynec Obstet* 1955 100 458.

[2] Lium, R. Maddock, S *Surgery* 1948 24 593

[3] Millbourn, E *Acta chir scand* 1949 98 1

[4] Warren K W *J Amer med Ass* 1954 154 803

[5] Dunphy, J E, Brooks J R Ackroyd, F *New Engl J Med* 1953 248 445

DIAPHRAGMATIC RUPTURE

THE diagnosis of traumatic hernia due to non penetrating injury is easily overlooked Most commonly the patient has received a crushing injury to the abdomen, so attention is directed more to possible visceral damage than to the abdominal parietes and chest Of the 7 cases seen by Evans and Simpson[8] 4 had fractures of the pelvis In the case reported by Dr Hamdi and Dr Sturdy elsewhere in this issue the patient appeared to have only a head injury, but while anæsthesia was being induced for reduction of a depressed fracture herniation took place through a diaphragm weakened by injury They agree with Evans and Simpson that a sudden explosive rise in intra-abdominal pressure, due to straining under the anæsthetic, can precipitate herniation This two stage mechanism—diaphragmatic trauma followed by herniation due to a momentary rise of pressure from below—can lead to further diagnostic difficulty since the two events may be separated by a considerable interval In 2 patients seen by Evans and Simpson six months and two years elapsed after the injury before the onset of symptoms, which in 1 case started quite suddenly while the patient was lifting heavy weights After such an interval the original injury may have been forgotten, and there may be no tell-tale scars to recall it Coincidental rupture of abdominal viscera is uncommon, and acute symptoms usually arise from displacement of lungs on the one hand and strangulation of abdominal viscera on the other In the case reported by Mr Sinha, also in this issue, the spleen was ruptured, but bleeding from it began only at emergency thoracotomy for reduction of the hernia Often, too, there is no pain referred to the shoulder, perhaps because the phrenic peritoneum is insufficiently irritated by a simple tear

Accordingly the diagnosis may be extremely difficult In a case lately investigated by a coroner[9] a young woman had received injuries to her face, body, and hip in a car crash After six days in hospital she was discharged, but returned almost immediately with internal hæmorrhage At laparotomy this was found to be due to recent ruptur of the splenic vessels, the spleen itself was intact, lyin within the abdomen, while stomach and colon had passd into the chest through a hernia in the diaphragm Radiography had revealed a diaphragmatic hernia which w regarded as congenital, and from the necropsy appearances it was concluded that the hernia was of long standing and probably congenital This may be another example of the double mechanism of a faulty diaphragm resulting later in expulsion of viscera into the chest

UNIVERSITY AND TOWN

FOR three days last month the University of Sheffie opened its doors to the people of the town Almost ever department in every faculty had prepared demonstratio illustrating the work they were doing In the faculty medicine, the department of medicine demonstrat the incidence of the killing diseases in a remarka cheerful way, and they allowed visitors to estimate t capacity of their lungs with a spirometer The departme of therapeutics and pharmacology showed some isoto techniques for measuring blood volume, and every could have an electrocardiogram while they waite Blood-transfusion work was vividly illustrated by th department of pathology, and the department of surgery had demonstrations dealing effectively with septic han arterial disease, and gastric acidity In the departm of obstetrics and gynæcology, the cycle of life, throu fertilisation, conception, and birth, was portrayed b models and diagrams

MEDICAL ASPECTS OF NUCLEAR RADIATON

THE membership of the committee on the medic aspects of nuclear radiation which, as the Prime Minist announced on March 29,[1] the Government invited t Medical Research Council to form, has now be announced The chairman is Sir Harold Himswort F R C P, F R S, secretary of the council, and the oth members are

Sir Ernest Rock Carling, F.R C S, F.R C P, consult adviser, Ministries of Health and Home Office (Civil Defen and member of the health policy committee of the Ato Energy Authority, Sir John Cockcroft, F.R S, director, Ato Energy Research Establishment, Prof Alexander Hadd M D, director, Chester Beatty Research Institute, J F Loutit, D M, director, M R C Radiobiological Research Un Kenneth Mather, D SC, F.R S, professor of genetics, Bi ingham University, W V Mayneord, D SC, professor physics applied to medicine, London University, P Medawar, D SC, F.R.S professor of zoology and comparativ anatomy, University College, London, J S Mitchell, M. F.R S, professor of radiotherapeutics, Cambridge University L S Penrose, M.D, F.R S, Galton professor of eugen University College, London, Sir Edward Salisbury, F. F R S, director, Royal Botanic Gardens, F G Spear, M. deputy director, Strangeways Research Laboratory, Ca bridge, J R Squire, F.R C.P, professor of experiment pathology, Birmingham University, C H Waddingto SC D, F.R S, professor of animal genetics, Edinburgh U versity, Sir Lionel Whitby, F R.C.P, regius professor physic, Cambridge University, and B W Windeyer, F.R.C professor of radiology (therapeutic), London University

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[6] Duval M. K Ann Surg 1954, 140, 775
[7] See Lancet 1954, ii, 1282
[8] Evans C J, Simpson, J A Thorax, 1950 5, 343
[9] Wales Guardian, March 18, 1955

[1] See Lancet, April 9 1955, p 768

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Special Articles

LEADERSHIP IN CARDIOLOGY *

The Charles Laubry Lecture

Sir JOHN PARKINSON

M.D Lond LL.D Glasg D.Sc N U I F.R C P
Hon. F.R C.P E Hon F.A C.P

 this lecture I am allowed to voice what is in my d and memory In my mind is the realisation that progress of cardiology has been mainly due to a ession of individuals who proved to be leaders in ught in action and notably in discovery In my nory is the state of medicine, including cardiology n I began as a young student fifty years ago and the nsformation that has since taken place I propose to ak on three separate subjects first of those early s and of that great leader James Mackenzie secondly specialism and the training of the cardiologist and rdly on French cardiology and the leadership of fessor Laubry

Days Gone By

May I look back at medicine as I found it in my own le at the London Hospital ? The study of the basic ences was limited to two years of inorganic chemistry sics, and biology Then followed two years of atomy happily under Arthur Keith while physi gy was too largely a system of conflicting hypotheses, ugh not for my own teacher Leonard Hill. All this ng over it was then our lot to live for as many hours possible with the sick in the wards and outpatient sics, learning by precept and practice what was ong with them and what to do for them We learned ly what our teachers knew except for what was in r textbooks, the most popular of which was Osler's o had no research consciousness though we were forced be clinically conscious In medicine our dozen teachers re equally chiefs ; but, looking back, how unalike their attitudes and talents ! Outstanding was Henry ad, an inspiring teacher but admittedly odd in having earch on the brain and even submitting to experi ntal operations on his own nerves Otherwise research d no place in the wards it was none of our business e were busy learning from our elders and there was a de variety of approach a wealth of practical experience those who moulded us One teacher one professor is ter enough the more the better—and often the rrier Among them was that fountain of clinical sdom, Sir Robert Hutchison who is still with us and o prayed From inability to let well alone from much zeal for the new and contempt for what is old ; m putting knowledge before wisdom science before art, verness before common sense from treating patients cases ; and from making the cure of the disease re grievous than the endurance of the same : Good rd, deliver us '

During my medical apprenticeship our clinical practice s mostly empirical and we were not bothered by hniques As a clinical clerk I did use the first sphyg manometer in the hospital and a thin X ray film uld drift into the ward though it might show little yond the fingermarks of the radiographer There was n no separate science of psychology but patients were ted and treated as kindly as today though with less derstanding for the state of mind of the sick was not lized. Sex did not exist as a subject to be taken into ount by all doctors I had read Oliver Wendell Holmes however and he said ' The sound of a kiss is not so loud as that of a cannon but its echo lasts a great deal longer ' There were two kinds of heart disease, valvular and non valvular and we were satisfied Digitalis was given for heart failure in the wards but forbidden to outpatients Antibiotics were scarcely on the horizon and infections ran their course Many physicians had lost faith in therapeutics and patients were pacified with traditional remedies culled from the hospital pharmacopœia

In those last fifty years, medical practice has become more rational while advance by experiment has largely replaced advance by observation yet there is still ample scope in clinical science for patient observation I have been impressed by the way that the science of mind, psychology has gradually permeated practical medicine. Doctors more often and more exactly try to realise in their own minds the position and feelings of their patients. This studied humanism has largely taken the place of what was called the art of medicine Indeed today we may speak more simply and truly of the science of medicine It has been said that he is the best physician who inspires hope, but too often he brought ' no other medicine but only hope no material benefit Comparing the past with the present it is surely in *treatment* that advances of the greatest magnitude have been made The medical profession is greatly strengthened by the good will and moral support of the community and nothing has elevated medicine in public esteem more than the spectacular progress in medical and surgical treatment in recent years.

Men and Heroes

How then has medicine and with it cardiology, grown ? It is surely a story of men It is biography It is the life and achievement of a succession of men and women—a few of them geniuses many talented and a host with fewer gifts but determined to use them well Thus in a volume like Herrick s *Short History of Cardiology* we read a story of persons and their ideas and achievements rather than a summary of theoretical and factual progress.

In our boyhood and youth we all had our heroes bright and shining maybe historical or fictitious or martial but scarcely political and not at that time medical. As we emerged from boyhood and came to the study of Medicine this hero worship was still strong in us persisting through our medical training ; and many of our teachers became and remain our heroes You will agree that this faculty of admiration hero worship can and often does persist and that it still exerts a power in our lives It has truly been said that we are a part of all that we have met

People vary a great deal in the way they allow others to influence them Many are self sufficient sure of themselves independent Incidentally it has always been a surprise to me that Americans, whom the world regards as particularly independent and insubmissive to authority should be so devoted to their heroes—national social and medical Despite their inveterate fondness for something new and their urge to pursue the impossible they are catholic in their search for truth and love of learning Nowhere have the famous physicians of the past and of every country been held in greater honour than in the United States

Sir James Mackenzie

May I now remind you of the life and work of James Mackenzie the centenary of whose birth occurred last year ? At the age of 25 he joined a busy general practice in Burnley a Lancashire industrial town where, for twenty-eight years he practised medicine midwifery and some surgery It was under these conditions seemingly so unfavourable for such work, that the greater part of his original observations and researches was made Up to this time neither he himself nor others had much confidence in his powers or promise, his was a brain that developed slowly The stimulus proved to be the shock of realising his ignorance, his inability to understand or deal with the painful problems that faced him daily. One such was the unexpected death in childbirth of a woman under his care from heart failure He could not understand how or why it had happened or how it could have been recognised in time Such events stirred him to discontent, and so he consulted books and journals but found no satisfaction He did not know It did not seem to be known He would find out We cannot doubt that deep feeling has often been the spring of medical research It may thus depend on a man's upbringing and character, and his devotion to an ideal So Mackenzie set to work to study common symptoms like fatigue, dyspnœa, and pain, and to learn their significance by noting their clinical course over the years Impatient only with his lack of knowledge, he patiently took notes and made records year after year with a sphygmograph and later with the polygraph he devised but in which he took little pride Here was a genius for taking pains but a common sense that kept technique in its place as a servant and not a master

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* rom the Charles Laubry lecture delivered at the 2nd International Congress of Cardiology at Washington D C on Sept 17 1954 The full text appears in the May issue of *Circulation* published by the American Heart Association.

It had always been assumed that pain and tenderness arose directly from an organ, but Mackenzie gave the first description of hyperæsthetic skin areas associated with disease of particular viscera He showed that pain and tenderness were referred from an organ to the spinal sensory centres and thence projected to the periphery Such a "viscero sensory reflex" explained the curious extensions of pain in angina pectoris At the same time and independently, Henry Head was elaborating similar views which were published a few months after Mackenzie's

Herrick, whose death this year we lament, wrote "It was largely through Mackenzie's influence that the term 'heart failure' lost much of the opprobrium that had attached to it" Indeed it was not regarded as a proper subject for clinical investigation until Mackenzie convinced the world that the subject of heart failure was of paramount importance in heart disease, and its prevention and treatment the ultimate goal A similar revival of hope resulted from his teaching, based upon long observations on sinus arrhythmia, extrasystoles, and on murmurs which were compatible with good health In a clinical sense he isolated auricular fibrillation, at least in its relation to failure and to its particular response to digitalis

In 1902 appeared that remarkable book *The Study of the Pulse* which had no wide circulation but was quickly seized by the discerning as proof that a great investigator had been quietly at work for twenty years In 1908 came his *Diseases of the Heart*, and in 1909 *Symptoms and their Interpretation*, which together showed Mackenzie to be the most original and vigorous mind engaged in this sphere, and people began to talk of the "new" cardiology What was new was the critical, the scientific approach, and the introduction of hope into what had seemed so largely hopeless

In 1907 he had left general practice for consulting and hospital work in London In a few years he became physician to the Cardiac Department of the London Hospital, where he continued his researches and influenced the many physicians who came to his wards As years went by, he was limited physically by angina pectoris and in 1925 he died in London from cardiac infarction

What kind of man was Mackenzie to meet? He was Scottish in appearance and in accent, a massive figure with a slight stoop His bearded face, with its large brow, was carried by a large and noble head His eyes were searching, twinkling and friendly as his face was lit by a gentle smile, though not too often In general he was serious-minded and looked it, but there was a simple blunt humour near the surface Socially he was warm-hearted without being genial He was gentle in his dealings with patients, especially women, more exa towards his assistants, yet appreciative Thus he wa mightily pleased with his first resident, soon to be k in the first world war, who took better polygrams th he could himself

Though not by nature of a pugnacious temperament he was a fighter for his opinions, and he had to be Th was little appreciation and some opposition from ma of the older physicians of his day I was warned of th risks I took by becoming his chief assistant What a universal change there has been in the common attitude towards what is new, when it is true, and for this I believe we have largely to thank the Americans!

Mackenzie, you will have gathered, found it hard to be satisfied, yet it was a calm and hard headed man wh carried that unquiet and inquiring mind More, he wa a happy man, secretly gratified by his achievements and their recognition, proud to have such friends as Cushny Keith, Allbutt, Osler, Wenckebach, and Thomas Lew and constantly sustained by the deep and abiding affection which existed between him and his wife

Specialism

The second of my three subjects is specialism and the training of the cardiologist

Specialism has been called the growing point of knowledge, and it is to specialism, disintegration in a sense, that the splendid advances of the last half-centu have been mainly due Though many have opposed i notice that no one has encouraged specialism, inde that would be superfluous in so natural a process remember well the time when medicine was held to be indivisible, and cardiology was not regarded as integral branch of it The word cardiologist was not use, or it was used unkindly, whereas today a cardiologi claims to be as truly a physician as any other The stoc criticism was that specialism engenders a narrowness view, bad for the doctor himself and for his patien But, as Hughlings Jackson said "There is no harm studying a special subject, the harm is in doing kind of work with a narrow aim and a narrow mind" cardiology, as in other branches, a new and broade outlook has developed, it becomes more and mo general The true specialist looks anywhere and every where for the means of cure and prevention All the physical, mental, and social factors relevant to his ow subject are considered and integrated by him as they never were before

In some quarters there are still attempts to fo trained and mature men to abide by the past custom claiming acquaintance with the whole of general medici But many young physicians are attracted by the wi scope and variety of service which a special study of th circulation and its diseases offers Medicine has divid It already has children—the present specialties, now the grandchildren, the subdivisions—perhaps to future specialties—are growing up around us Nor parents take pride in their offspring and are particula tolerant towards their grandchildren The subdivi or differentiation, which has come to pass in medi as a whole, is now affecting us in cardiology An inst is vascular disease, and the programme of our cong proves the fact, for it is full of diverse subjects or specialties

As a cardiologist, my personal attitude towards furth specialisation can be simply stated Each individ should be allowed to make his own choice, as he did w he chose the profession itself Naturally he will seek consider advice from his teachers though he is no at school He may misjudge his own ability or the for his particular endeavour, but he has a right to ch the road he will take A wise man—and that could a young man—should recognise his limitations, bu must follow his bent The public is aware that scular disease is predominant in human mortality edicine has always been influenced by public opinion nd patients will surely claim the services not only of neral cardiologists but also of special cardiologists who ave exceptional experience in one variety of circulatory sease.

raining the Specialist

The serious danger of specialising too early is universally dmitted and it is effectively disallowed in our institu ions But how long should the training in the sciences nd in general medicine be followed after graduation? Dare I suggest that for the future specialist it may ometimes be too prolonged? Life is short For how ong should an ophthalmic surgeon restrict himself to eneral surgery and for how long should a young urgeon remain in general surgery before concentrating is powers and gaining experience in cardiac surgery? imilarly a young physician—adequately trained as uch—may prejudice the fullness of his career if he post pones for too many years the plunge into what is to be his ife-work. So let us give greater individual choice as to hich branch of medicine he favours and even, with the afeguards already mentioned as to what stage in his areer he begins to specialise. I would hesitate more to ake this unorthodox suggestion that specialisation may egin too late if I did not know that there is often a ome-back a natural return to greater commerce with eneral medicine as a man proceeds in his career

ompulsory Research?

Happily there are plenty of men you cannot keep om original research almost or actually bloodthirsty their pursuit of it others only need putting on the cent and they're off on 'the track of Truth" But ust every ambitious graduate be forced by custom or uthority to prosecute research in order to obtain a niversity post or to succeed as a practising cardiologist? esearch ability used to be regarded as a rare gift some hing of a phenomenon. It was search with some prospect f finding; it connoted both a spirit of curiosity and a apacity for investigation That is not the attitude day, though one must admit that it is largely the pansion of organised research that has transformed edical practice My question concerns the universality the capacity for research and I almost believe that e true investigator great or small is born not made hat famous literary physician Sir Thomas Browne, rote: 'Every man is not a proper Champion for Truth r fit to take up the Gauntlet in the cause of Verity' ere is a matter of policy and procedure in our profession hich will have to be decided. In my view we encourage od men inapt for original research to sacrifice their me and energy upon it when they should be perfecting emselves as bedside physicians Are we losing our sense proportion exhilarated by the wonderful products of cent and current research? Is a born investigator a perior being to a born clinician and teacher? He may may not be Advances in medicine comprise two parate stages: first the discovery of something new d valuable as a result of investigation secondly the plication of that new discovery to the benefit of the dividual patient The same man may not be the right e for both stages though he can be

Though commoner than aptitude for research the wer to apply new (and old) knowledge judiciously is t given to everyone It also requires a gift—namely inical judgment This will ripen to clinical wisdom ly by constant association with the sick Young ysicians of this type—so badly wanted—need to keep emselves abreast of the world literature in their ecialty, and devote time to postgraduate clinical work other centres and in other lands Must they invariably forced to shorten the time required for this large rpose to participate in minor and often ephemeral research before they are considered for any important staff appointment as a teacher or consultant? Not every young physician or cardiologist should be under compulsion to prosecute individual research in order to succeed.

It would not be surprising if the magnitude and the magic of recent advances went to our heads The secret places of the heart are probed or rendered visible. The blood is directed where it may run and under orders when it may clot now even its channels are to be kept clear of their silt But after all scientific truth is dis covered not created by us and knowledge is not always progress Some will remember the warning given by Professor Laubry at the European Congress of Cardiology in 1952 about the peril of technical dogmatism and the need to retain a measure of salutary doubt There is always a limit to scientific certainty in medicine, and some humility of approach is therefore becoming In fact, it is probable that we are producing both truth and error as our forbears have done The circus theory of auricular fibrillation for example seems to have come and gone but happily no patient has been allowed to *suffer from this physiological disaster!*

Research Applied

The original worker in research is fully aware of the importance of his subject and cannot be held back Are we as aware of the immediate importance of that other pressing duty that of applying the safest and soundest treatment to the sick of today? I mean getting it applied more certainly and more universally If our minds are possessed by the greater things research will do for them in the problematical future, we may be less mindful of the mass of human illness requiring our best endeavour today The vision of new truth should not blind us to our bounden duty as doctors Any hospital may be proud of the amount of research being conducted within its walls But it should be equally proud of a reputation for applying—in current practice to the patients under its care—the sum of accumulated knowledge, the best treatment in the world today In this connection may I venture the opinion that the governing bodies of teaching hospitals would be wise to retain on their staff and value the services of an adequate number of practising physicians These should not be sacrified at the altar either of science or of uniformity with loss to medical education and to the community Indeed, a medical staff will never be uniform, and the establishment should always be flexible enough to fit the exceptional individual and the late-developer and to take full advantage of any new perhaps unexpected, discovery

Unity and Friendship

I have touched on several problems for which, I doubt not solutions will be found or will naturally emerge Meanwhile we must be prepared for change willing to allow our younger gifted men freedom to strike out on their own lines according to personal inclination and judgment The call is to adapt ourselves to the changing form that cardiology is taking rather than to attempt to maintain its earlier compactness or to keep a strict symmetry in our organisation If only we cultivate the good feeling so evident at our congress we need have no fears for the future. Most of all the bond of unity will continue to lie in the grandeur of our purpose—namely the prevention relief, and cure of cardiovascular disease

When one speaks of unity and of leadership your thoughts will go at once to the president of our congress Dr Paul White Friendship for a country rests largely on personal friendships with its citizens. On that basis though not solely I would pay my tribute to the lead taken by the United States in the realm of cardiology and also give thanks for the close friendships which have bound me to this great country He spoke of hero worship, and Paul White remains one of my abiding heroes A counterpart to Osler in medicine, he has been an ambassador of good will and good hope to cardiologists all over the world He has made many original contributions, and by means of his famous book he has proved a trusty unseen consultant to countless doctors In it he has reverently combined a choice of the past with the best of the new

The French Contribution

Finally I want to say a little about the course of cardiology in France in recent years Following Potain there has been an unfailing sequence of distinguished cardiologists among French physicians First came pure clinicians like Merklen and Huchard, but it was the work of Vaquez, who combined the traditional French *clinique* with the physiological methods and researches of Marey and François Franck, that marked the beginning of contemporary French cardiology Apart from Laubry himself, to whose achievements I will return, we record with admiration the fine influence of Clerc, the brilliant observations of Gallavardin of Lyons in clinical cardiology, and the example of Giraud Then I would draw your *attention to the constancy and the quality of the work of* Professor Lian, a physician remarkable for his clinical discernment These have been followed, in strength, by Souhé, Lenègre, Froment, Heim de Balsac, Routier, and others

Inspired by the work of Helen Taussig and Blalock, and by their auspicious visit to Paris in 1947, Professor Donzelot and Professor d'Allaines, physician and surgeon, have combined in the last few years to make an important contribution from the cardiac centre at the hôpital Broussais This year, that work has been published by their brilliant co-workers, in particular Heim de Balsac, as a *Traité des maladies congénitales*, a large volume richly illustrated, and perfectly produced That is true also of another up to date French treatise for reading and reference, *Électrocardiographie clinique* by Lenègre and his colleagues

The contributions of France would be more widely evident today if it were not for the unfamiliarity of the English speaking countries with that graceful language We should all gain by a hearty understanding with France, a medical *entente cordiale* The place of France in the civilised and cultural world cannot be shaken by the passing effects of war or by political vicissitudes

Too often Paris has been solely a place for sightseeing and gaiety, and that was largely true in my own case On an early visit, however, I was privileged to go round the wards with the great Vaquez, who was attended most devotedly by his *chef de clinique*, no other than Laubry himself As Evan Bedford has said, " The great traditions of the Paris school of cardiology have been handed down in direct line from master to pupil for over a century, starting with Corvisart and passing in turn to Bouillaud, to Potain, to Vaquez, and finally to Laubry " Tradition may be a source of strength and a justification for authority To Laubry was bequeathed that authority and we realise today how valuable it has proved for the continuity of French cardiology under the trials of recent years Notice that he has been content to make this branch of medicine his life work, and the chair of clinical cardiology in the University of Paris was created for him

To begin with, he has been a brilliant clinical teacher, directly influencing students and graduates from the whole continent of Europe and elsewhere Lenègre has described those fascinating bedside clinics by the *patron* as reaching the unity and the charm of a *cardiological* ballet—though he allows that sometimes there might also be a display of fireworks !

Then since 1936 he has been the director of the *Arch* [illegible] *maladies du coeur*, founded by Vaquez in 1908. In the following year, he founded the Society of Cardiology Lastly, he has steadily tributed original research by way of clinical intuition synthesis combined with precise laboratory methods The work of his pupils bears testimony to his leadersh and the important theses produced year after year und his direction indicate the scope of his interests and h capacity for guidance His son, Dr Pierre Laubry, h also made valuable contributions

Professor Laubry has methodically assembled his knowledge in book form In 1921, he published Pezzi, a treatise on congenital heart disease In 1 appeared his famous *Leçons de séméiologie cardiovascu* and in 1930 his large textbook on heart disease O of his favourite subjects has been gallop rhythm, which he wrote, with Pezzi, a valuable monogra Interested by Vaquez and Bordet in cardiac radiolog he instituted with Chaperon a long and painstak research on the radiological anatomy of the heart great vessels, normal and pathological, using ra opaque injections The results appeared in two la volumes in 1939, *Radiologie clinique du coeur et des vaisseaux* by Laubry in collaboration with Cotte Routier, and Heim de Balsac *It has provided a scienti* basis for cardiovascular radiology ; in particular, t composition of the vascular pedicle and the lung shadows was elucidated , and you will remember concept of the small aorta—large pulmonary artery 1950 appeared the second edition of *Les maladies coronaires* with Souhé, a comprehensive and mod textbook In the same year, to the amazement of thos who had not appreciated the depth of his scholarship, for he carries his learning lightly, came his own tra lation into French of William Harvey's *De motu cor* (1628) We in Britain especially value this tribute fr one we are proud to number among the fellows of th Royal College of Physicians which the illustrious Harv himself adorned

The outcome of a man's life may be measured by ratio between his natural gifts and opportunities, and th service that he dedicates to the common good You w agree that it is not only his talents but the use he h made of them that has won for Professor Laubry th unique position in the cardiological world He posse all the elements of greatness, and they are still after an unusual experience in living, for he has pa his 80th year *In his long pilgrimage*, by teachin research, and personal example, he has set himself quicken and confirm progress in the wide realm of car vascular disease, so that he has provided a verita pattern of leadership

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PREVENTION OF JUVENILE DELINQUENCY

Two types of children come before the juvenile co —mischievous young law breakers and unhappy prob children Sir BASIL HENRIQUES, who classified them this way when giving the Peter Le Neve Foster lect at the Royal Society of Arts on April 27, finds weakest part of child-welfare work in England to be preventive side

Many of the children born between 1939 and the of the war were separated for years from their pare and lived among strangers When the time came return, their mothers had become strangers and som times the children now had less liking for their mot than for the foster-parents they now had to leave Wh their fathers came back from the Forces they too become strangers—*not only* to the children but times also to their mothers and the strangeness of parents to one another was as devastating to the chil- as their own strangeness to their parents Some of mothers had acquired new interests and did not welc back with the love and enthusiasm about which had been long day-dreaming and some of the rs brought an almost military discipline into the e, while some were over indulgent The war, in fact uced not only many problem children but many lem parents

e mischievous young law breakers Sir Basil finds ordinary boys with plenty of initiative and courage no proper outlets for their high spirits (This has the experience of other observers: John Barron s[1] noted that Liverpool boys often commit offences ly because they need to prove their courage to one her) Only some 46% of those committing crimes is country are detected, and every young delinquent rally expects to be among the 54% who are not ht Three things, Sir Basil suggested are needed revent those crimes of adventure: first a police brought up to full strength and with better methods etection secondly enough playgrounds and sports nds for children and young people; and thirdly ortunities for them to spend their leisure in a useful constructive way He believes that the various youth nisations could give them such opportunities, but these organisations are chiefly handicapped by lack eaders of the right kind Pearl Jephcott,[2] however er study of membership of youth clubs found that about 1 in 3 children join clubs—and these are not ssarily the children who would profit most from n. Green spaces sports gymnasium and boxing ht attract more of those who now fail to join but at ent few youth organisations can offer all these things

THE UNHAPPY CHILD

ut it is not in Sir Basil s view, the adventurous child much as the unhappy disturbed unsettled child who ents problems to the juvenile courts Lack of rdination between the various agencies dealing with rived and difficult children often results in failure to e action as soon as anything amiss is noticed in child amily He spoke warmly of the example of New South les where every aspect of child welfare comes under ministry which has concentrated on preventive rk Juvenile welfare in our own country is parcelled among the Home Office and the Ministries of ucation Health and Labour

Abnormal behaviour in a child nearly always means t he is unhappy at home and many people have the nce to see his symptoms—the health visitor the ing manager the staff of the nursery school or day sery his teachers in his primary and his secondary ools the leader of his play centre his officers in the bs and Scouts his club leader the youth employment ficer and (at every stage) his neighbours Some of se watchers are bound to realise when all is not well th him; but they are not clear what to do about it d often nothing gets done

He quoted the case of two little girls now aged 5 and 6 ose mother had died two years ago and whose father had en as his second wife a girl who had absconded from a ony of mental defectives Since there were now two rents to look after them the children (who had been in the e of the local authority) were sent home The teachers their school noticed that they lost weight and seemed iously hungry and put them on school dinners. In the ter weather at the beginning of this year they came to school ly shod and in cotton frocks. They often said that they re frightened of their father and asked leave to keep their ts at school lest he should destroy them One afternoon y cried hysterically and refused to go home and their cher called in the police and had them brought before the rt as in need of care and protection

Thirteen months earlier the health visitor had referred case to the National Society for the Prevention of Cruelty to Children; and neighbours had also reported to the society that the children were never allowed to play in the street but were confined in a small back yard where there were rats If they were naughty they were put in a corner of the yard, and, if they moved the dog of which they were terrified was let loose

Sir Basil pointed out that the children's officer the school care committee, the education department and the after care officer for mental defectives (who was supervising the stepmother) all knew about this family yet these children had been allowed to suffer for many months without remedy

A CHILD WELFARE OFFICE ?

He suggests that we should establish in every town and in every district of cities, a child welfare office to which anyone concerned about the well being of a child can go for advice and guidance It should be a building worthy of its purpose presided over by the children's officer as director of child welfare and it should contain the headquarters of all the statutory and voluntary bodies which deal with the welfare of children This is no mere dream, for in Manchester many of the voluntary agencies concerned with children already have their offices in the same house The juvenile court he thinks should hold its sessions in a room in the child welfare office—a suggestion which would not win the support of C A. Joyce headmaster of the Cotswold School, who believes that the juvenile court ought to impress the child, not give him the idea that whatever antisocial thing it was he did hardly matters. The great advantage of housing all the welfare agencies under one roof of course is that a family needing help can be referred at once to the appropriate body Thus parents persuaded to consult the probation officer could do so on the spot before their moderate ardour for his advice had time to cool

FAILURES IN PREVENTION

One great weakness in our present system Sir Basil thinks is the relatively slight attention we pay to absenteeism from school yet this is a sure sign of something wrong somewhere School inquiry officers are among the most poorly paid of local authority servants They should he suggests be highly trained family case workers employed not by the education but the children s department and it should be their job to discover the real reasons why the child is staying away—the negligence of the mother or her demands for the child s services in the home or the child's own failure at school which has led him to play truant Moreover if he was a trained child welfare officer teachers would tell him not only about absentees but about children sent to school dirty or persistently late children showing behaviour problems, and children, lately cheerful who have become sullen and morose

Sir Basil spoke of our failure to prevent some of those who leave borstals or approved schools from committing further delinquencies—blaming a system which reforms the child and sends him back to the unchanged home conditions under which he broke down Work on the family of a child or young person committed to a school or borstal,' he says, should commence the very day he enters the school. He proposes that all children under 15 who need residential training should be committed to the care of the local authority this would place the local authority *in loco parentis* until the young person reached 18 Approved schools for children under 15 would under this arrangement become members of a pool of ' residential schools' ; and the local authority could send the child to the school appropriate to his needs—whether it was one specialising in delinquents or an ordinary school As no authority would wish to have more children in care than necessary, there would be an incentive, at present lacking, to get the home improved as quickly as possible This proposal has all the charm of orderliness , but it is hard to be sure that the irresponsible parents would really benefit from having their duties taken over by the local authority , or that the child would gain in security from learning that he was no longer under the control of his parents It is a situation calling for much careful thought

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[1] Growing Up in the City Liverpool 1954 See *Lancet* March 5 1955, p. 503

[2] Some Young People London, 1954 See also *Lancet* loc cit.

A MINISTRY OF JUVENILE WELFARE ?

Finally Sir Basil would like to see the children's department of the Home Office, the Ministry of Education, the National Youth Employment Council of the Ministry of Labour, and the department of the Ministry of Health which deals with children of school age and under, combined to form a Ministry of Juvenile Welfare, *a minister of Cabinet rank* This idea too has attractio its weakness is that it separates the child's situation that of the family as a whole—and this, as we are and painfully learning, cannot be done Perhaps one towards a coordination of services is to begin at the ot end, as the *Times* (April 28) suggests, by training a set of "general-practitioner" family case workers, replace the multiplicity of inquiring people now visiting the homes of families with problems Like her counter in general medical practice, she would be able to ca just the agencies which could help, thus coördinat their efforts from the start.

Public Health

THE POLIOMYELITIS-VACCINE CONTROVERSY

FROM AN AMERICAN CORRESPONDENT

The announcement on Franklin D Roosevelt's birthday of the effectiveness of the Salk vaccine in protecting against poliomyelitis was greeted in the United States with great satisfaction both by the lay public and by the medical world Since then there has been a tremendous hullabaloo which has been and is being stoked up by the press, radio, television, and the Poliomyelitis Foundation For one thing, there has been an argument about the distribution and use of the vaccine, and this has been engaging the attention of the United States legislative bodies, organised medicine, the trade unions, and the pharmaceutical houses The public want the vaccine "for free" (as they say) they have contributed generously year after year to the March of Dimes fund of the Poliomyelitis Foundation and they feel that they have bought their share of this advance On the other hand, the pharmaceutical firms need to recover their investments and wish to make a profit for their stock holders, while doctors, with no national health service behind them, quite properly want to charge for giving the injections

Much more disturbing was the announcement that poliomyelitis had developed in a number of children who had had vaccine prepared by the Cutter Laboratories, and this vaccine was withdrawn from general use While the facts and the possible explanations have been presented at length in the press, a much quieter scientific controversy was going on, and this has been brought into the limelight at the annual meetings of the American Society for Clinical Investigation and the Association of American Physicians which were held last week at Atlantic City Dr Jonas Salk and Dr Albert Sabin have long held opposing views about vaccination against poliomyelitis For many years they have presented their hypotheses at medical meetings , but this year they came up with facts, and it looks as though Sabin may be right He favours the use of attenuated-virus vaccine given by the natural route of infection (by mouth), while Salk believes that formaldehyde killed viruses given parenterally will produce antibodies as effectively as and more safely than modified living viruses Sabin has contended that intramuscular injections of killed vaccine will not confer lifelong immunity and that it would be impracticable to re vaccinate each time the short lived artificial immunity runs out If children received such a short term vaccine, he argues, there would soon be a population of young adults with no protection against poliomyelitis , and as the disease is more severe in adults than in children, a vaccine which confers only a short immunity might eventually result in many severe illnesses when [illegible]dren grew up This situation is already developing for a different reason in the United States Great Britain, for example, where standards of hyg are high and natural infection is therefore relati uncommon The exact duration of immunity confe by the *formalin killed* vaccine cannot yet be known. Salk has suggested, on the basis of studies on a lim number of subjects, that the immunity will be life-lon

Salk's short paper given at the annual meeting of American Society for Clinical Investigation was his *presentation of data collected from last year's huge* test of the action of polyvalent vaccine in prod antibody in children Three serial injections were g and antibody titres were measured at frequent inter before, during, and after the vaccinations The first vaccinations were given close together, and the or "booster" injection a variable time later Sa found that the immunological response to poliomy virus antigen in man was made evident by two measu reactions—the antibody response itself and the sta hyper reactivity to subsequent antigenic stimulation. the hyper reactive state there was a shorter inte between provocation and secondary antibody resp and the secondary response was very much greater th the primary one The degree of the secondary resp was shown to be influenced by the intensity of prim stimulation, the intensity of the secondary stimulat and especially by the interval between primary secondary stimulation The full secondary effect in could not be elicited unless the secondary stimulat was given several months after the primary inject These factors were also found to influence the degre which the serum antibody levels tended to pe Immunological response in man, following injection non-infectious poliomyelitis virus vaccine, was affe by previous immunological experience with one or of the three types of viruses, responses being striking with previous exposure to type III virus. also suggested that the presence of *measurable* amo of circulating antibody in children may not be an esse prerequisite for immunity to paralysis In some chil no antibodies were found in the blood , yet they respo to the primary injection by a rapid rise in antibo which persisted in the blood It seemed clear that t children had been previously exposed to natural p myelitis without getting paralytic disease Salk sp lated that the hyper reactive state was an impor protective mechanism against natural poliomyelitis. believed, on the basis of this work, that natural rea tions with poliomyelitis after invasion through natural portal of entry, will stimulate promptly formation of antibody and thereby limit deeper inva or further multiplication of the virus The ex question of life-long immunity could not be answe at present

Sabin, who is director of the research unit of Children's Hospital of the University of Cinc Medical School, presented his investigations to the A ciation of American Physicians He has devel *mutant attenuated strains* of virus which, when g himpanzees by the natural oral route provoked the elopment of antibodies in the circulating blood and erred 'life long' immunity to the three types of lytic poliomyelitis virus The chimpanzees had no gnisable illness as a result of exposure to the atten d virus and these viruses have never reversed their ations to reappear in the virulent paralytic form for chimpanzees Sabin described a dramatic experiment 1 20 young volunteers in the Federal reformatory at llicothe, Ohio Varying doses of living attenuated is were given to the men in a drink of milk and ibody titre was measured serially Repeated cultures e collected from the mouth throat and fæces tibody formed rapidly, and has so far persisted in blood Virus could not be recovered from the mouth, was recovered from the throat and fæces With ge doses of virus the stools have remained positive up to three months The minimal dosage was 01 ml of the pure culture This amount of virus voked excellent antibody response when swabbed on throat of the volunteers. No illness appeared in any the volunteers nor in the men who were in close tact with them in the reformatory Sabin stated t when comparative studies had indicated the best ains to use, it would be possible to determine whether not the optimum attenuated poliomyelitis virus—her given in milk or simply swabbed on the throat—ld be used for primary immunisation or for production an effective type of immunity in individuals temporarily tected by natural antibody or non infective vaccine

It was clear that many doctors at the meetings feared t the public had been too readily convinced that liomyelitis had been conquered For there are many ering facts for example quite apart from any estion of infective batches of vaccine many vaccinated ldren will get poliomyelitis for the Francis report de no higher claim than that the vaccine was effective 60–90% of those who received it

Issue of American Vaccine Suspended

Further supplies of poliomyelitis vaccine will not be ued in the United States until an inquiry into manu turing standards and safety tests has been completed nouncing this on May 6 the Federal Surgeon General, Leonard Scheele said that the vaccine was still ing produced but Federal approval of additional pplies was being held up for several days.[1] Scheele was testifying before the banking committee the House of Representatives on pending bills that uld give the government power to control the price d distribution of the vaccine. He was confident that experts now examining the situation would conclude at the vaccine was excellent and that vaccinations ould go on It would be decided in the next few days ether the vaccine would continue to be tested by spot ecks as at present or whether every lot should be amined Dr Scheele said that on May 6 the total cases of poliomyelitis in newly vaccinated children s 41 of whom 38 had been given Cutter vaccine ked whether this vaccine was now suspected he olied : We have to have a lot more evidence before could decide [2] Since April 1 he said there had en 389 cases of poliomyelitis in the United States, mpared with 423 in the same period last year

In a report issued two days later Dr Scheele announced at a detailed reappraisal of each lot of vaccine already eased or in final stages of production was being dertaken[3] He hoped that vaccine would be available use again by the end of this week There had been cases of poliomyelitis among more than 5 million ople vaccinated, and if only 1 in almost 700 000 ildren inoculated with vaccine from companies other an Cutter Laboratories had incurred paralytic polio yelitis Dr Scheele added this meant there was every ason to believe a product of the other manufacturers is safe He said there was a definite association between the Cutter vaccine and the cases of poliomyelitis that had developed after its use So until the precise cause was found the vaccine produced by this laboratory would remain suspended

The Medical Research Council has sent a member of its staff to the United States to obtain first-hand information. This should be available before the routine safety tests on the present batches of vaccine are completed and therefore before any proposed trial in this country is due to begin Meanwhile, the council will continue with the arrangements for starting the trials.

Cadmium Poisoning

The industrial diseases subcommittee of the Industrial Injuries Advisory Council is considering whether cadmium poisoning should be a prescribed disease under the National Insurance (Industrial Injuries) Acts, and if so for what occupations. Industrial injuries benefit can already be claimed for acute cadmium poisoning as injury by accident. The committee are inquiring into the possibility that prolonged exposure to cadmium at work can give rise to chronic ill health against which insurance cover should be provided Persons and organisations interested in the question of prescribing cadmium poisoning are invited to submit written evidence Communications should be addressed to the secretary, Industrial Injuries Advisory Council, 10, John Adam Street, London, W C.2 to arrive not later than June 6, 1955

Infectious Diseases in England and Wales

Disease	Week ended April				
	2	9	16	23	30
Diphtheria	8	5	7	14	9
Dysentery	1869	1457	1191	1053	879
Encephalitis :					
Infective	4	4	6	3	3
Post-infectious	4	2	5	0	3
Food poisoning	156	180	158	135	177
Measles excluding rubella	32 324	30,885	32 980	28 474	22 637
Meningococcal infection	11	30	28	36	38
Ophthalmia neonatorum	43	46	30	48	44
Paratyphoid fever	17	13	2	16	15
Pneumonia primary or influenzal	1050	872	804	668	610
Poliomyelitis					
Paralytic	5	3	14	1	9
Non paralytic	1	4	0	5	10
Puerperal pyrexia	224	213	253	220	270
Scarlet fever	824	666	607	707	461
Smallpox					
Tuberculosis					
Respiratory	704	614	609	88	867
Meninges and C.N.S	13	14	17	21	20
Other	65	61	50	76	80
Typhoid fever	2	4	[illegible]	3	
Whooping-cough	1842	1310	1471	1664	1768

Not including late returns

Medicine and the Law

State of Doctors' Surgeries

Two decisions by the London Executive Council at its meeting on April 28 concerned the duty of practitioners under the National Health Service to provide and to permit the inspection of proper surgery accommodation Clause 7 (4) of the Terms of Service requires the practitioner 'to provide proper and sufficient surgery and waiting room accommodation for his patients having regard to the circumstances of his practice Clause 7 (5) provides that on receipt of a written request the practitioner shall at all reasonable times admit any member or officer of the council or the local medical committee authorised by the council for the purpose of inspecting the surgery or waiting room.

In the case of Dr A an inspection was made in February, 1955

Dr A's surgery hours were from 11 A.M to noon but when the inspecting officer called at 11 40 A.M., Dr A who apparently slept in the consulting-room was not ready

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1. *Times* May 7 1955.
2. *New York Times* May 7 1955
3. *Times* May 9 1955

to receive patients In the waiting room was a quantity of old paper, a dilapidated leather trunk and a tin box The consulting room was in a state of muddle - The floors had no covering and had not been swept The visit was paid when there was snow on the ground, but there was no evidence of a fire in the waiting room, although Dr A said that a fire was provided when required There was no running water in the consulting room and no light in the lamp holder in the waiting room, and in both rooms the windows and curtains were dirty

Dr A was invited to submit observations and to attend a meeting of the medical service committee He failed to do either The executive council adopted a recommendation that representations should be made to the N H S tribunal that the continued inclusion of the practitioner in the council's medical list would be prejudicial to the efficiency of the service

The case will now be subject to inquiry by the tribunal

In the case of Dr B the local medical committee had asked for an inspection of the surgery and authority had been given by the chairman of the council

Dr B agreed to receive the inspecting officers and the hearing was fixed for March 11, 1955 Dr B subsequently wrote stating that the date was inconvenient as decorations to the premises had not been completed and the council to defer the inspection until the middle of The council replied that they had not asked that the should be re decorated before inspection. Dr B was that the duty of the inspecting officers was to report to council on the present condition of the premises and that information he gave as to re decoration &c, would incorporated in the report The apparent reluctance of doctor to permit the inspection of the premises was to the notice of the appropriate committee on March and on the following day the doctor was notified that committee had decided to refer the matter to the med service committee unless he indicated several days the ensuing fortnight on which the surgery could inspected No reply was received from Dr B

The medical service committee considered that had shown a complete disregard of his obligations the Terms of Service and they advised that a recom mendation be made to the Minister of Health the sum of 30 guineas be withheld from his remunera The executive council adopted this recommenda which is subject to appeal

Parliament

Review of Social Services

IN the House of Commons on May 4 Dr EDITH SUMMERSKILL, in opening a debate on the social services, regretted that the report of the Phillips Committee on the economic and financial problems of the provision for old age, had been ignored by the Government She pointed out that the new scales would not help the old-age pensioners on National Assistance Of those on sickness benefit 123,000 would only get 2*s* 6*d* extra, and most of the people receiving this benefit were the chronic sick This led her to ask the Minister of Health if he was satisfied that, having regard to the hardship it imposed, and the administrative burden it entailed, the shilling prescription charge should be continued? Had the Minister inquired in districts where industrial processes had a deleterious effect on the workers' teeth to see whether withholding a free service had resulted in a deterioration of dental health? She understood that £50 million was spent annually on drugs, 30% of which went on proprietary drugs She found it difficult to understand how the Minister could allow this huge sum to go on swelling the large profits of the big drug houses, knowing how cheeseparing he was in other directions The Minister had been trying to persuade doctors to use cheaper alternatives, but he had done everything except take strong action He should refuse to sanction unnecessary expense in prescribing when there was a satisfactory alternative

Mr IAIN MACLEOD interposed that Dr Summerskill's suggestion might infringe the right of a professional man to decide what, in his judgment, was best for his patient Though advice had been given to doctors that certain drugs were not of proven therapeutic value, if a doctor in his own discretion still decided to prescribe one of them it was perfectly legitimate for him so to do

Dr SUMMERSKILL went on to ask if the Minister thought he was justified in allowing hospital beds to be earmarked for fee-paying patients when in some districts there were long waiting-lists, and whether he could report any improvement of conditions in our mental hospitals

Mr OSBERT PEAKE, Minister of Pensions and National Insurance, described the Phillips report as "most valuable" and said that it was clear that as a result of it there would have to be legislation at a later date amending the National Insurance scheme But he thought the scheme was a good one and he would be reluctant to introduce changes into it just for the sake of changes He had been assured by the National Assistance Board that the increases in February had fully restored the loss of purchasing-power of the allowances which had occurred since June, 1952 In July, 1948, the Assistance Board were paying 842,000 allowances, that figure had risen by the end of March, 1955, to 1,807,000 increases in pensions would reduce by 100,000 the num going for assistance

Mr KENNETH ROBINSON returned to the case of boy with a fractured and dislocated arm who had wa at Hampstead General Hospital for more than six before he received medical attention Mr Rob had found the Minister's reply about this case satisfactory[1] But the matron immediately began give interviews to Press reporters in which she said she had not heard of anyone being reprimanded explained that the boy had been kept waiting for hours because it had been impossible to get a spec in the hospital sooner, and that he had not been food or a sedative because he was to have an anaesth Mr Robinson shared the great respect and gratitude the House and the country had for the nursing profe but it seemed to him that some members in the hi ranks of the profession were rather resentful of crit The matron of this hospital had in effect repudiated Minister's apology and Mr Robinson felt that the could not be left there

Mr MACLEOD agreed that Mr Robinson was to raise this case in the first instance and, in view of statements which had been made, he was wholly rig raise it again He, like Mr Robinson, had hoped with the full apology which he had made on behalf the board of governors, and in particular on of the Hampstead General Hospital, the matter had closed He had been considerably startled to read in newspapers the comments which the matron had The answer which he had given to the House on was made after consultation with the board of gov and it had the agreement and encouragement of people responsible From time to time one got impression that the people concerned in these were a little reluctant to admit that they were in because they thought that might reflect upon a ho of which they were *rightly proud* In his view that a wrong attitude If a fault was found, nothing hospital more credit than to say that it was and it was right that an explanation should be frankly to the House of Commons by the Mi *responsible, as had been done in this case* hospital had slipped in one particular instance, it did mean that it was not a fine hospital with fine as he was quite certain was the case here We all adm the quality of loyalty and he could easily under a matron who was proud of her hospital and the working there resenting, perhaps a little too any suggestion that the hospital had slipped in its But what had been said was unwise and unf it should not have been said, and he was certain that matron much regretted having made an allegation he understood she had—against Mr Robinson himself

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1 See *Lancet*, May 7, 1955, p 966

urning to the question of prescribing, Mr Macleod l that it was entirely within a doctor's discretion to scribe a particular drug even though it had been gested by the committee and Ministry that this was advisable He would not be surcharged for that was possible—and this was a different point—that his scribing as a whole might be looked at, and one element ght be the over-prescribing of one particular drug Macleod did not see how they could achieve what Summerskill seemed to have in mind which was ited to the prescribing of the ordinary substances on the list without interfering with the ordinary clinical eedom of doctors He would not wish in any way to terfere with the right of a doctor to prescribe at his scretion in individual cases The total bill for England and Wales for medicines was about £43 million not luding hospitals, and within that sum £21 million a little more than half was due to proprietary medi es. That was cost alone the non proprietary pre iptions would be more than half because the others re more expensive Many of the greatest discoveries, h as the antibiotics, had been made by private firms garding the pattern of dental treatment, Mr Macleod d that the important fact was that conservative atments had gone up from 4 070 000 in 1951 to 00,000 in 1954 that in the school dental service the mbers, which had fallen at the end of 1951 to 713, d risen at the end of last year to 979 The dental atment of the priority classes was a great deal better in it had ever been

About 1% of the beds in the National Health Service re private beds and about a third of those at any given e were occupied by non-paying patients, either on unds of medical urgency or to see that the beds were ed The proposal to abolish pay beds was a breach faith with millions of people who paid into contributory emes so that they might have some privacy in spital.

The mental hospitals had no waiting list, and the 8500 ls that were being provided were a contribution to the ef of overcrowding For the mental-deficiency pitals there was a waiting list of about 7000 5007 ls had been completed, or were nearly complete l there were also 945 beds included in the 1953–54 gramme, not all of which could be actually occupied There was therefore a programme of at least 0 beds as against a waiting list of something like 0 But the Government had recently announced substantial hospital building programme and the ntal-deficiency side would get its full share

Prison Reform

In the House of Lords on May 4 Lord PAKENHAM in ling attention to the Prison Commissioners report for 53 said that he had lately shared in an inquiry, under en on behalf of the Nuffield Foundation into the es of crime, and in the last year or two he had ited some 20 prisons or borstals. He submitted that xt to nothing was being done to reform the majority convicted prisoners indeed it might well be argued at they were likely to come out of prison worse than en they went in We were not making an effort in a direction commensurate with our degree of social lightenment in other fields

The overcrowding of our prisons—the fact for instance, at out of 17 485 in prison 2880 were still sleeping three a cell—was a sore impediment to the best intentioned ison staffs. The most troublesome bottleneck which day frustrated the efforts of all who would like to extend e training system using that word in the sense not ly of trade training but also of moral training was e shortage of staff Today the three-shift system was force in only a quarter of our prisons But without the idea of individual treatment for prisoners would main a fantasy It was a major and imperative duty ther to bring down sharply the number of prisoners to increase rapidly the number of staff

Viscount TEMPLEWOOD pointed out that only 21 000 en and women were involved Surely a welfare State ith all the immense improvement that we had seen in ery social service could deal with this small problem an urgent and common-sense manner Yet instead of progressing, so far as accommodation and work went we had fallen back 50 or 60 years. He urged that there should be an inquiry into all prisoners records to see how many of them could be allowed to work outside prison Work in prison should be useful and paid for at regular rates. The money should be allocated to the man's keep, compensation for the victims, and the provision of a sum for the prisoner when he left prison The best hope for many offenders was to make them work and make them take an interest in it Lord MOYNIHAN suggested that there should be compulsory aftercare for boys of 14–17 who were sent to detention centres He would like to see the system of ' home leave extended and given not only to those who had happy homes but also to the homeless He was sure that carefully selected families would be prepared to take these boys in the first weeks of their probation The appointment of permanent welfare officers in prisons would be a great step forward

Lord MANCROFT, joint parliamentary under secretary of State for Home Affairs, said that the prison and borstal population in 1930 was 10 000 and by 1952 at the peak it had reached 24 000 Since then it had gradually decreased and was today about 21,000 The effect of the sharp rise was that in 1952 there were 5200 prisoners sleeping three in a cell That figure was now down to 3000 Nothing but necessity excused that deplorable state of affairs Oddly enough, this situation had had little effect on health and discipline, but it remained wholly undesirable Overcrowding was not allowed to interfere with training in specialised prisons; its effects had been confined to local prisons. The plans for new prisons were based on the bold decision to break away from the traditional walled prison and to place in open conditions all who could safely and properly be trained there. There was *no shortage of men coming* forward for posts as prison officers, but they were not always the right men Recruits were urgently needed There had been a shortage of work in the prisons, but the past year had shown improvement In all specialised training prisons there was a full working day in good class industrial work. The treatment of prisoners was now dominated by the conception of training The Government stood by that conception and believed it to be wholly right and proper

Full use was being made of the detention centres by the Courts, and it was hoped to widen the system The centres were making an effective contribution in combating juvenile delinquency Many prisoners who had otherwise been written off as hopeless had been saved from a life of crime by flexible methods of corrective training Greatly increased medical services had been set in progress since the war in local prisons, directed towards rehabilitation—particularly psychological and psychiatric services rehabilitative surgery and specialised treatment under the National Health Service, both in outside clinics and in hospitals While there was still great room for improvement there had been a great effort to improve the Victorian sanitary conditions in prisons and this effort would be continued The whole process of aftercare for prisoners other than in local prisons, had been reorganised by the formation of a Central After Care Association, and by the decision to bring in the probation officers as field workers for the association Every prisoner in the care of the association after his release was under the immediate supervision of a skilled social case-worker

QUESTION TIME

Review of Extraction rates of Flour

Replying to a question Mr HEATHCOAT AMORY Minister of Agriculture and Food said that he had decided in conjunction with the Secretary of State for Scotland and the Minister of Health to arrange for an independent authoritative review of the scientific and medical evidence now available in regard to this matter Lord Adrian president of the Royal Society had nominated for the conduct of this review the following panel of representatives of scientific and medical opinion:

Sir Henry Cohen F.R.C.P., Professor of Medicine University of Liverpool (chairman) L J Witts F.R.C.P., Professor of clinical medicine, University of Oxford J H Gaddum, SC D, M R C S F R.S, professor of materia medica University of Edinburgh A C, Chibnall SC D F R.S, formerly professor of biochemistry, University of Cambridge R A Morton D SC., F R.S professor of biochemistry, University of Liverpool

The terms of reference of the panel are

In the light of the scientific and medical evidence now available to determine the differences in composition and nutritive value between (*a*) National flour as defined in the Flour Order 1953, (*b*) flour of extraction rates less than National flour as defined in the Flour Order 1953 to which the three token nutrients have been restored (*c*) flour of extraction rates less than National flour as defined in the Flour Order 1953, to which the three token nutrients have not been restored and to advise whether any such differences are significant from the point of view of the health of the population

Poliomyelitis Vaccine

Replying to a question, Mr J R BEVINS, as representing the Lord President of the Council, said that the current programme of poliomyelitis research coördinated by the Medical Research Council might show whether there was any practicable alternative to the use of monkeys in preparing a poliomyelitis vaccine, but he was advised that an adequate substitute for monkeys was unlikely to be found in the near future for a vaccine of the Salk type It was hoped, however, that adequate supplies of monkeys would be available again shortly He could give an assurance that research to find a promising substitute was going on Before any of this type of vaccine was used in this country it would be very carefully tested on monkeys or some other animal

Replying to a further question, Mr MACLEOD said that recently reported events in America were being fully considered by the M R C, and a member of their staff was going over there immediately to get first hand information This should be ready for study here before the routine safety tests, now being conducted on batches of vaccine, were finished and therefore before any of the proposed trials on children over here were due to begin Meanwhile arrangements for these trials continued There was no intention of inoculating any child unless the full consent of the parents had been first obtained

Postal Votes

Replying to a question, Mr IAIN MACLEOD said that he had studied carefully the documents sent to him about pressure being brought to bear on doctors by local Conservative associations to send them the names and addresses of their sick, blind, and aged patients for the purposes of the postal vote It was desirable that everybody should be aware of their right to a postal vote and equally important that any information given should be made available to all political parties who asked for it There was nothing wrong in responsible citizens, doctors or others, bringing to the notice of those concerned, whatever their politics, their rights as postal voters On the specific question about extracting patients' names from doctors' lists, he would not expect information concerning doctors' National Health Service patients, which was normally regarded as confidential, to be disclosed for some entirely different purpose He was sure that doctors understood the position and that no special communication was necessary

Welfare Foods

Replying to a question, Miss PATRICIA HORNSBY SMITH gave the following figures for the distribution of welfare foods

Welfare food	1953 July–Dec	1954 Jan –June	1954 July–Dec
National dried milk (millions of tins)	12 34	11 92	11 33
Cod liver oil (millions of bottles)	3 28	3 30	2 79
Vitamins A and D (millions of packets)	1 03	1 03	0 83
Orange juice (millions of bottles)	15 58	14 81	13 41

These foods, she added, were intended for those whose diet might otherwise be deficient, and the arrangements of the local authorities were well adapted to concentrate attention on this group In the community as a whole the downward trend might well continue with the continuing improvement in the general diet and standard of living The department would maintain a close watch on developments

In England Now

A Running Commentary by Peripatetic Correspon

To conduct, control, and conclude a consultati a querulous, persistent patient is an exercise in ap personality that can be fascinating to the be although arousing different emotions in the p Medical students may study their chiefs and in outpatient departments the patients may fill the waiting time by making extensive observations on th subject I have had the good fortune to purs subject under both conditions and here pres preliminary report

The commonest method, and one lacking all cha to terminate the interview and stop all further que is " I'll write to your doctor You go round and disc it with him next week " The psychiatrist, and those wit psychiatric leanings have an altogether more diplom approach, an approach designed to act like foam on fire, to damp down and smother the burning passio and to allow those that will not be smothered to bu themselves out These experts just let the patient on talking and talking while they remain emotionle impassive, impersonal, and aloof At the end of th allotted hour they quietly make an appointment for further instalment, no doubt noting in their notes "M Next Week " Another subtle, though somewhat approach is to appeal to the patient's self-esteem by flattery This is often successful with readers of popu medicine articles You merely have to preface yo remarks with " A man with your knowledge of medic will at once realise " Another convenient form for the rushed doctor, but one liable to cause addictio and even abuse by the lazy, is the " Let-me-know-if gets-any-worse " approach This is of course not fo proof, for next week the patient may return to sa that it has become worse Under such conditions anoth line must be taken. One may assure the patient th he has a very rare, interesting complaint for which yet there is no treatment (this is much favoured b neurologists), one may keep them under observatio (a physician's gambit), or one may adopt the "Tha funny, I have the same trouble myself," and the unload your anxieties and symptoms upon the pat Oddly enough this seems to help both the patient an the doctor

* * *

We are once again in the midst of an election batt with all parties in search of the elusive floating vo and I am irresistably reminded of the last electio and Annie

Annie was one of several hundred old dears at home for the aged Never very active, she was confined to bed permanently with gangrene of foot, which she stubbornly refused to submit to surger She lay there in gloomy silence, and appeared to ha abandoned all interest in life

Which party it was, I forget, but some shrewd politi type saw in the home a happy hunting-ground for vo A fleet of cars arrived, and all those passed as "f were taken to the poll. Annie pleaded for a ride, I hadn't the heart to refuse

On her return she was in a state of considerable tion " I do hope I done right—I suppose it's all for best " The old dear commented so seldom upon thing that such concern over the election was ext ordinary Sister investigated Annie was quite sure had just given consent for her leg to be amputated

I often wonder for whom she voted

* * *

As our taxi hurtled over the perilous track to Bab we found the driver glad to talk of life in his count We passed a convoy of army trucks given by the Un States and mobile A A guns made in England, then army camp Oh yes, there was national service, he sa two years for all men—unless they paid 50 dinar which case it was three months That is official dinars secures complete exemption That is unoffici We skidded and slid in the sand, bumped, and thump our way from one mud hollow to the next, and stil smiled and joked. There was the way trucks are overloaded (nearly everyone we saw was an example) When the last bus home was full the driver sent his colleague on to the roof among the luggage. But that night it was windy and cold so he shared a coffin with its rightful owner on his way to his burial When the next man came up on the roof the living occupant of the coffin put out his hand to show he was there He went to court—not for travelling with a corpse in a coffin but for putting out his hand in such a way as to frighten the newcomer Three months jail was the price of his thoughtlessness.

"We are living in the 10th century here our driver said as our 20th-century limousine survived mile after mile of insult. Wives are still cheap 60 dinars buys the ordinary kind 100 the very best If the husband does not like her he kills her She was no good' in the law courts means no worse a penalty than two months in prison That is the law, you see." What happens if a man murders another man? we asked Oh he is hanged of course," he replied

Wives do the work while husbands sit in the cafés smoking their great ' hubble-bubble ' pipes. Toiling in the fields on either side of us through the hours of light were these poor peasant women heavily clothed in tattered black. There, too, were superb birds feeding in freedom Large green bee-eaters swooped on flying insects blackwinged stilts probed the saltings with their graceful bills a solitary flamingo stood still. 'If I d had the chance before I was born to choose what to be, I d be a bird, he said I see what he meant.

* * *

My peripatetic colleague surely cannot seriously intend that we should instruct our adult patients to Lie on the couch with your tummy upwards.' But I agree that the usual ' Lie on your back on the couch ' regularly results in a patient lying on his face The remedy came to me in a moment of inspiration: 'Lie down on the couch please. I say no more no less I have yet to see a patient who spontaneously adopts any but the supine position

* * *

Last year our rural district almanack and directory had some interesting health notes and hints for the nursery

Headaches, dizziness and shortness of breath are often caused through neglecting the feet

"Cramp generally arises from a disordered liver For quick relief from the pain the feet should be plunged into hot water and rubbed hard with a towel. If hot water is not obtainable rub in camphor liniment or embrocation.

"If a person cannot sleep it is because blood is in the brain; the remedy therefore is to draw blood down from the head. This may be done by eating one or two small onions or a biscuit

"It is harmful to force a baby to take notice The brain will develop much better if left naturally

"Paddling in the sea is a serious danger to many children. Paddling has been known to cause convulsions, cramp heatstroke and severe bronchitis

Unfortunately the publisher seems to have had a hint that the notes are a little outdated for this year they have been replaced by notes on bird life and a page of wit and humour

* * *

In bed with another overpowering cold I am feverishly wondering why this type of coryza major never afflicted me until I came to British Columbia But here of course the forest trees are enormous, the buttercups grow twice as high as those in English meadows, and gigantic salmon throng the rivers. I ought to have known that the viruses would be jumbo size

* * *

Psychiatrists must look to their laurels, for it seems that their closed shop is not so closed as they think. In the last issue of *The Lancet* I read of kidneys showing "a diffuse distal tubular neurosis Imagination boggles at the future Are we to hear of neurotic syndromes relating to all histologically differentiated regions of the body? Sorry Old Man can't play golf today, I ve neurosis of my islets of Langerhans

Letters to the Editor

BLOOD-AMMONIUM LEVELS IN LIVER DISEASE AND "HEPATIC COMA"

SIR,—In their article (April 23) Dr Phear Dr Sherlock, and Dr Summerskill have shown that the administration of ammonium chloride and methionine to two patients was followed by gross mental deterioration culminating in coma They state (p 838):

> As in case 1 *therapeutic* [my italics] administration of ammonium chloride caused the blood-ammonium level to rise before clinical deterioration took place and again recovery coincided with a fall in the blood-ammonium level. Following oral *dl* methionine a relapse was associated with a rise in the blood-ammonium level

The manner by which this information was obtained raises moral and ethical questions. No doubt the relationship between the level of blood-ammonium in liver disease and the production of mental changes is important to medicine. However, this information had already been obtained by other workers to whom reference was made in their opening paragraph (p 836) In order to prevent a premature or rash judgment on the moral issues involved would Dr Phear and her colleagues be good enough to answer the following queries

(1) Did they know that ammonium chloride and methionine were potentially dangerous to cases 1 and 2 before the drugs were administered? If they did why was it necessary to confirm the knowledge?

(2) Were the patients consulted before substances potentially dangerous to them were given and did they agree to participate in the experiments?

(3) If the patients did agree were they capable of fully understanding the nature of the therapeutic experiments and the dangers involved? From figs. 4 and 5 it would appear that they were not mentally normal before the noxious substances were administered

(4) If one of the patients had died in coma during the therapeutic trial would the coroner have been informed and given the full story?

(5) Would they have performed similar experiments on themselves or on their near and dear ones supposing they were clinically suitable?

Medical research workers who are concerned with human lives have to steer carefully between the production of fruitful work and the obligations of the Hippocratic oath In this spirit, I look forward to a satisfactory reply

Pathology Department,
Birmingham Accident Hospital

S SEVITT

*** This letter has been shown to the authors of the article whose reply follows—ED L

We are glad to answer Dr Sevitt's points

1 Ammonium chloride (in the management of ascites) and methionine (on the nutritional hypothesis) are currently used therapeutic agents in the treatment of liver disease. Our paper concerns therapeutic trials *not* experiments Ammonium chloride and methionine were administered to these individual patients in order to diagnose accurately their mental and neurological illness. As we have concluded in this paper there is no certain biochemical method of diagnosis, and transitory mental and neurological deterioration after methionine ammonium chloride or a high protein diet are the only certain diagnostic tests we know Simple protein restriction is not a certain diagnostic method for we have observed patients with chronic portal systemic encephalopathy who have failed to respond to it. The diagnosis of these complications can be extremely difficult and later experience makes us think we may have over-simplified the issue in our earlier paper (*Lancet* 1954 ii 453) Certain diagnosis can of course be followed by correctly applied treatment Trials of this nature in patients with obscure mental and neurological illnesses will prevent many being admitted as certified insane to mental hospitals We have recently known of

six such instances We also give courses of ammonium chloride and methionine to candidates for porta caval anastomosis, where the development of mental or neurological changes contra indicates the operation It is unjustifiable to perform this operation without such a preliminary trial

2 The patients were aware of the nature of the substances they were to receive (they had had them before therapeutically in other hospitals), and that it was necessary for diagnosis to determine their effect They knew that temporary mental and neurological deterioration might follow, and willingly agreed

3 They were capable of understanding the nature of the trial

4 Under conditions of careful observation by the team here (which includes a full time trained psychiatrist alert to the earliest mental changes in liver disease), the possibility of permanent sequelæ or fatal issue due to these drugs is non existent The changes are transient and reversible The coroner would of course always be informed of unexpected death during any treatment

5 If we or our relatives suffered from liver disease and had mental changes or had an obscure organic psychosis or neurological illness it would be necessary, under hospital observation to determine the effect of nitrogenous substances including ammonium chloride and methionine

Dr Sevitt rightly emphasises the moral and ethical issues involved in our efforts to diagnose our patients' ills and in attempting to define more accurately the management best suited to their needs Like other members of our profession we are constantly guided by these moral obligations to patients who have sought our help or have been referred to us as difficult problems It was this moral obligation which prompted us to report our observations in the medical press and thereby draw attention to this complex and ill-understood aspect of liver disease This may provide guidance for others in the diagnosis and management of obscure organic psychoses, prevent unnecessary certification, and possibly prevent the present abuse of a high-protein diet and other nitrogenous substances in the treatment of liver diseases

We will be pleased to meet Dr Sevitt so that we can discuss the matter more fully and perhaps show him the clinical management of patients with liver disease in this hospital

INSTINCT AND THE NURSING COUPLE

SIR,—I would like to congratulate Dr Mavis Gunther on her interesting observations on nipple protractility, in her article of March 19, and to concur entirely when she says that, in human mothers, instinct does not ensure maternal efficiency in breast-feeding

This is perhaps made more obvious by the present day contrast between the high incidence of failure in the West and the almost universal success amongst tropical peasant mothers For example, in Yorubaland in Western Nigeria, of 208 children aged between one month and two years who were investigated, all were found to be still breast feeding successfully[1] Similarly, an as yet incomplete infant feeding survey in rural West Bengal has shown uneventful and continuous breast-feeding in all of over 150 infants aged between one month and thirty months so far investigated—with the exception of a small number where death or very severe illness of the mother made breast feeding absolutely impossible In both of these surveys, a high proportion of the nursing mothers were markedly malnourished

As to the factors suggested by Dr Gunther as being responsible for success or failure of breast feeding, I would offer the following comments and additions

(i) *Instinctive response*—This certainly appears to predominate in the infant rather than the mother, but the newborn baby will have more chance of successfully making contact if he is lying on a mat by the mother's side with the breasts near at hand, as occurs with the tropical villager

(ii) *Learning by observation*—From infancy Asian and African peasant females are surrounded by women unconcernedly and unashamedly breast feeding their children, not only in the house, but anywhere and at any time of the day or night

(iii) *Psychological factors*—The Western woman frequently approaches breast feeding not only in ignorance of practical details, but often with some, at least, of the following psychologically disturbing attitudes a fear of failure (engendered to some extent by modern old wives tales), a clear knowledge that easily accessible alternatives are available (which have been drummed into her since childhood by ubiquitous advertising), a desire to return to work or social life as soon as possible, and sometimes a dislike of the whole process or even in extreme cases an alleged disgust All of these can interfere with the mother's confidence and ability, so that, as stressed by Verhœstraete,[2] the disastrous snowball effect of worry—poor "let-down" reflex—dissatisfied baby—increased worry, &c occurs, associated with a diminishing output of milk from inadequate mammary emptying By contrast, the tropical peasant woman (and her Western cousin until quite recently) approaches breast-feeding not with confidence, because this is too positive a word, but a completely matter of fact naturalness Without being conscious of it she knows from personal observation that breast feeding is a simple process carried on uneventfully, while, at the same time, her attention has not, as yet, been distracted by the advertising of artificial foods In this context, it is interesting to note that, according to Cicely Williams (personal communication) European women, pregnant when interned by the Japanese, were later all able to breast feed their babies when faced with the uncompromising reality of a Singapore internment camp

(iv) *Shape of breasts*—Dr Gunther's investigation of nipple protractility is of great interest As far as I am aware no investigation of breast or nipple shape or size has been carried out amongst tropical peasant women My impression amongst West African women was that, possibly as a result of a lack of any type of support, the breasts were somewhat pendulous even before childbearing Certainly after the first baby the breast becomes flat in the upper half and rounded and pendulous below, presumably partly as a result of uncontested gravity, so that babies can easily be fed per axilla when carried on their mothers' backs In these women the nipple protractility should, one would have thought, have been excellent and have acted as a good "sign stimulus"

It is also interesting to note that the aboriginal Juangs of India divide female breasts into different groups according to their alleged milk giving potentialities[3]—from the *latop nunoro*, which is flat like a tortoise and has a poor yield, to the *bagh nunoro*, the rounded, so called "tiger breast" which is reputed to have an abundant and easy flow One wonders whether there may be some association in this classification with nipple protractility and ability to act as a "sign stimulus"

To close this short picture of the contrast between the over sophisticated Western mother and her counterpart in the tropical village, I cannot do better than quote Matthews's excellent description of the latter as seen in Nigeria

"Her hormonal mechanism is undisturbed by anxiety complexes She is not besieged by friends, relatives, nurses and doctors advising her against breast feeding and putting her 'at the mercy of the accumulated gossip of her time' She does not receive, within a few days of confinement suggestive pamphlets from infant food manufacturers encouraging early weaning, nor is the Yoruba neurotically prejudiced against the nursing experience as being 'messy' and 'disgusting', nor does modesty prevent her feeding her baby in the markets, by the road side or, if she be a nurse, in the anteroom of the hospital ward What does she care if she lose her figure and her vein marked breasts sag near her umbilicus? Parenthood is her central interest, duty and pride"[4]

D B JELLIFFE

Calcutta

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[1] Jelliffe, D B Malnutrition in African Mothers, Infants and Young Children Report of 2nd Inter African Conference (C C T A) on Malnutrition London 1954 p 230

[2] Verhœstraete, L Epidemiology of Breast feeding (in the press)

[3] Elwin, V *Man in India* 28 1 Notes on the Juangs 19

[4] Matthews, D S *J trop Med* (in the press)

MEDICAL TELEVISION PROGRAMMES

SIR,—I protest against the programme shown on the B B C television service on May 2 Some elementary physiology was demonstrated with living subjects but the whole presentation was to me revolting At the point where a demonstrator actually burned with a lighted cigarette the forehead of a subject lying on a couch and connected with wires and tubes to recording gear, I switched the set off with the unanimous consent of my family Surely horror comics have nothing on this programme for pseudoscientific sadism

I hope there will be no more of this sort of stuff on television and that doctors will not coöperate in pandering to the crude public taste for medical sensationalism

Birmingham 15 FAUSET WELSH

HARDENED FATS AND LUNG CANCER

SIR —Dr Nyrop's further letter (April 23), erudite though it is should not be allowed to divert your readers from his original and quite unwarranted contention He has sought to show that a deficiency of essential fatty acids may be a factor in the causation of lung cancer and, more especially, that such a deficiency may be induced by the replacement of butter by margarine in the diet.

Something may be said for the introduction of new theories of carcinogenesis, in that they may stimulate useful lines of investigation But as regards the essential fatty-acid content of margarine we are dealing with fact not theory The fact is that it has been shown by animal experiment[1] that margarine contains a substantially greater amount of biologically active essential fatty acids than butter Dietary deficiency in these substances whatever its rôle in carcinogenesis is therefore *less* likely to occur when margarine is eaten instead of butter

Queen Elizabeth College
London W.8 JOHN YUDKIN

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[1] Deuel, H J., Greenberg S M., Anisfeld L., Melnick D *J Nutr* 1951 45 535

ELECTROPHORESIS OF PLASMA-PROTEINS

SIR,—In view of Dr J A Owen's letter of April 23 I feel I should point out that results of a rather similar nature have also been observed in these laboratories details of which will shortly be published in the *Journal of Clinical Pathology* There are, however some points upon which I would like to comment

We do not obtain such distinct double β globulin bands as is illustrated by (*a*) in Dr Owen's letter, unless the serum or plasma is fresh and unless the buffer contains borate Dr Owen's result, in the absence of borate appears to be the exception rather than the rule as is evident from the great majority of published illustrations of paper electrophoresis of sera in Veronal buffer

The reason for the occasional exception is not at present clear; we confirm that the slower β globulin component is undoubtedly labile as it disappears after serum has been allowed to stand at room temperature for several hours or even after storing at −20°C for two weeks. Borate appears to exert a stabilising effect in electrophoresis, but in the absence of borate there may be other factors in Dr Owen's experimental condition which also prevent alteration of the labile component. Contrary to Dr Owen our results suggest that the labile component is converted in aged serum to one of higher mobility and merges with the normal faster β-globulin band.

In his second illustration (*b*) there is also shown a double β band, but in this case the slower component is absent and a band appears just ahead of the normal β band We suggest that this faster component is an artefact produced presumably by enzyme action on one of the β globulins since we have obtained similar results only with sera which have been aged at room temperature for long periods

Alterations in the ratio of the concentration of the two β globulin components in fresh serum or plasma may well be significant in some diseases but it is clearly important that no appreciable alteration to the unstable component should occur during electrophoresis One method would appear to be the use of borate, but in borate alone α_1 globulin has a *mobility similar to that of albumin* This disadvantage has been overcome by employing a mixed borate veronal buffer, which is now being used in these laboratories for routine investigation Full details will be published in the forthcoming paper

Canadian Red Cross Memorial Hospital,
Taplow Maidenhead, Berks. R CONSDEN

A MORPHOLOGICAL CRITIQUE OF TEMPORAL LOBECTOMY

SIR,—In his article (April 30) Dr Crome expresses doubts regarding the validity of the biopsy findings reported, among others in a paper by myself in collaboration with Mr Murray Falconer and Mrs Elizabeth Beck.[1]

> In this paper we discussed rather fully the difficulties inherent in the interpretation of biopsy material, and we had taken care to reduce the element of ' subjectivity by controlled serial investigations We also admitted to being inevitably handicapped by not knowing whether similar changes are found in the unoperated temporal lobe or in other parts of the brain In our conclusions which were mainly concerned with aetiological problems, we stressed the preliminary nature of our report and the importance of systematic post-mortem studies of clinically and electrophysiologically well investigated cases of temporal lobe epilepsy as ' they are bound to give a more comprehensive and clearer picture of the histological changes than the investigations of isolated biopsy specimens so difficult to interpret could ever provide '

Such post mortem studies on an adequate scale will naturally take some time to mature Dr Crome's otherwise important and interesting material is deficient *in this respect* since on his own admission no reliable information could be obtained on psychomotor phenomena hallucinations, and auras owing to the severe mental retardation in the majority of his cases.

The histological abnormalities in our material of 18 cases were severe in 11 consisting either of focal lesions (circumscribed tumours and vascular malformations) or of diffuse cortical and white matter sclerosis Partly overlapping with these cases Ammon's horn sclerosis was found in 7 (not 5 as Dr Crome stated) out of 12 cases in which hippocampal tissue was available for study Dr Crome dismisses Ammon's horn sclerosis as a merely secondary phenomenon due to severe grand mal or other types of anoxia Although we agree with this view (as we have been at pains to point out in our paper) this does not preclude its primary significance in the clinical manifestations of temporal lobe epilepsy Evidence has been accumulating particularly from experimental studies that Ammon's horn and the neighbouring uncus and amygdaloid complex serve general visceral function and have some relation to behaviour particularly emotional behaviour Their pathology in cases of temporal lobe epilepsy requires, therefore our earnest consideration

In only 4 of the 18 cases doubtful and uncertain pathological changes predominated although even in these some positive findings were recorded There is thus in our material considerable variation of the pathological changes both in quality and quantity as we stated in our paper Should these be causally related to the clinical manifestations of temporal lobe epilepsy this relationship would not be a simple one Perhaps we did *not* sufficiently emphasise this complexity in our *preliminary* communication but it has been given attention in our more recent publication[2] in which we discussed the possible significance of a genetically determined epileptic factor and of an unspecific *effect* of the operation by removal of not necessarily diseased centres and interruption of neuronal pathways responsible for the seizure In focusing attention on the complexity of the problem Dr Crome's paper has been very helpful.

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[1] *J Neurol Psychiat* 1954 17 [illegible]

[2] Falconer M. A, Hill, D Meyer A., Mitchell W., Pond, D A *Lancet* April 23 1955 p [illegible]

The modern concept of temporal-lobe epilepsy was evolved in the late 1940's chiefly on clinical and electroencephalographic evidence Anterior temporal lobectomy was introduced mainly on these grounds and, whatever the histopathological verdict, it will continue as long as the therapeutic results justify it

Department of Neuropathology,
Institute of Psychiatry
Maudsley Hospital,
London, S E 5

A MEYER

CIVIL SERVICE MEDICAL APPOINTMENTS

SIR,—It was with the gravest disquietude that I read the recent advertisements in *The Lancet* to recruit doctors to posts within the Civil Service

Perhaps the most glaring anomaly in these advertisements is the statement that there are "promotion prospects," this statement appearing with surprising regularity in every post that is offered This would indeed be a welcome change of heart if it were so, but when the Treasury evidence to the Royal Commission in relation to the claims of the Civil Service doctors is studied the statement becomes ludicrous

Perhaps the intending applicant has not yet studied this evidence, which indicates fairly forcibly the poor opinion the Treasury holds of us doctors in the Civil Service, and they are the people who count when the question of numbers and remuneration of higher posts is under consideration

The additional information given to candidates with the application forms is no more informative regarding these "promotion prospects" A small paragraph states quite simply that certain grades exist, but it does not mention what we all know—that all these posts are filled and any promotion is unlikely in the foreseeable future

It appears to me that this should be made known to intending applicants, for the impression given by the advertisements is far removed from the situation as we know it

TOAD BENEATH THE HARROW

A LIVER POISON WITH UNUSUAL PROPERTIES

SIR,—I have read with interest the letter on icterogenin by Professor Rimington in your issue of April 9, and I am sorry that I did not know of his isolation of the lippia poison when I wrote my first letter I am glad to hear that studies of the icterogenic properties of this remarkable substance are already planned May I suggest some points which I feel are of special importance in further studies with icterogenin ?

Firstly, it seems to me important to decide whether icterogenin jaundice be a retention jaundice or a lymphogenous jaundice The poison may act in one of two ways (or perhaps in both of them) (1) by paralysing the bile-pigment excretion through the parenchymal liver cells, and (2) by reversing the secretion of these cells from the normal pathway (blood to bile capillaries) to an abnormal pathway (blood to lymph capillaries) [1 2a]

This may be decided experimentally by collecting the liver lymph (or thoracic duct lymph) during icterogenin poisoning and determining the concentration of bile pigment at different times and comparing it with that in the serum If the possibility (1) is correct a prompt direct diazo reaction in the serum (which is found in lippia poisoning) occurs without the bilirubin having passed the liver cells, and if (2) is correct the existence of a secondary secretory mechanism as pathogenesis of lymphogenous jaundice is proved [1 2a]

If (1) is correct our concepts of retention jaundice must be altered Up to the present our knowledge of experimental retention jaundice has been gained exclusively from studies on partial and complete removal of the liver—a technique which is far from ideal because the removal of the liver is followed by important changes in many vital functions and especially because bile pigment production in the stellate cells of Kupffer, which seems to form the bulk of the bile pigment in higher animals,[2b] is abolished

In this respect it is important to remember that the jaundice of acute yellow atrophy of the liver is accompanied by prompt direct diazo reaction [2c] In this condition all parenchymal liver cells must be considered necrotic or at least completely inactive, while the stellate cells of the liver are relatively unimpaired [2d], so the jaundice in acute yellow atrophy seems to come close to a pure retention jaundice, and thus to be very similar to icterogenin jaundice if possibility (1) is correct As the two conditions have the prompt direct diazo reaction (van den Bergh) in common, (1) cannot be excluded beforehand

If possibility (1) be correct our theory of jaundice must be altered because, according to current concepts, retention jaundice can only become intense after several days [2e], and this cannot be so if lippia jaundice is a pure retention jaundice, because it reaches high intensity in two to three days Perhaps the high bilirubin levels in occlusive and parenchymal jaundice may be explained by retention without regurgitation or other forms of lymphogenous return of bile pigments to the blood.

Secondly, studies in as many species as possible including both laboratory and farm animals and birds, and, if feasible, volunteers, are highly desirable

County Hospital,
Svendborg, Denmark.

TORBEN K WITH.

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1. With T K *Acta med scand* 1947 128, 25
2. With, T K Biology of Bile Pigments Copenhagen 1954, a, pp 113, 122 b p 61 c, p 201, d, p 63, e, p 121

ENURESIS

SIR,—This correspondence and a sentence in your leading article of Feb 19 ("We are not so well equipped to treat enuresis that we can ignore any promising technique") prompts me to write of some conclusions I have formed from twenty years of dealing, in the main successfully, with enuresis in children

Does not the cause of our lack of success lie in the tendency for the specialist to treat enuresis as a phenomenon of the urinary system alone, and for the general practitioner to take the opposite line and tell the mother that the child needs no help and will "grow out of it" ?

It is, of course, true, as you state, that in a certain proportion of children the situation arises from specific pathological conditions of the urinary system, but these cases amount to a very small proportion of those suffering from this very common complaint Elaborate urinary investigations, on the other hand, tend directly to increase the child's difficulties in gaining control, and to hinder the achievement of understanding by physician, mother, and child of the part played by delayed bladder control in any individual child

Surely the kernel of the whole problem lies in the power of the body to use its normal functions both to side-track and express emotional strains ?

Do we not all remember the frequency of our visits to the w c while waiting for *viva voce* examinations, and have we not noticed how the frequency and timing of micturition in ourselves varies with the weather and the emotional significance of the day's programme ?

This ability of the bladder to respond to factors affecting the whole personality is much more marked in children than in adults There is, also, an aspect of urinary performance additional to the emotional factors described by other correspondents, which is peculiar to children

The adult is used to himself and his physical apparatus he has, alas, in most instances, long ceased to "play," and his excreting organs are only of passing interest to him On the other hand, in children, curiosity, the desire to experiment, the enjoyment of "play," and the urge to acquire knowledge of himself and his functions, and of the mysterious lacks in his small sisters, leads to a concentration of interest on his excreting organ which can be overlaid with other activities during the day, but returns with full force when they vanish in sleep Then, the child who is disturbed in his personality, as described by Dr Symonds (Feb 26) and who has insufficient opportunity and/or ability to make friends" with the varied aspects of himself, and to gain release from tension in play, will use his urinary function to achieve this end in sleep

It is not the bladder or its controlling mechanism but the ole child who needs investigation and help

The difficulty in the treatment of enuresis arises from the paration between pædiatrics and child psychiatry so at the pædiatrician too often sees only the function and e psychiatrist only the personality and such common nse factors as maturation opportunities for play and nsible education of the mother in understanding both des of her child's nature so often do not appear at all

It has been our custom in our treatment at the Institute Child Psychology to provide a ground floor room with cement floor sloping to the outside with illumination from waterproof ship side lantern which is fitted with sinks at ifferent heights, water toys of all sorts and pots and jars nd hose-pipes. Here clothed in wellingtons and mackintosh child can work out in real water the drives fantasies and xperiments and—with the aid of the therapist—clarify he puzzles which lurk in his mind and perhaps tip the balance owards expression of all these through his own water reserves t night

As Dr Jackson (April 16 p 822) has so wisely pointed out rate of maturation varies enormously in different children (though surely he is incorrect in putting the lower limit for bladder control at three years ?) and giving up the desire for elementary water play is a function of maturation.

Institute of Child Psychology,
London W 11

MARGARET LOWENFELD

THE DIFFICULT APPENDIX

SIR,—Mr Kerr ends his interesting article of April 9 with the sentence I have regarded McBurney's point as $^1/_2$ in. below the midpoint of the line joining the umbilicus to the right anterior superior iliac spine.

This implies that there is some choice as to where McBurney's point may be placed This is not true as is shown by the following quotation from McBurney's original paper[1]

> And I believe that in every case the seat of greatest pain *determined by the pressure of one finger* [italics by the author] has been very exactly between an inch and a half and two inches from the anterior spinous process of the ilium on a straight line drawn from that process to the umbilicus. This may appear to be an affectation of accuracy but, so far as my experience goes the observation is correct.

An asterisk after this sentence points to a footnote which reads as follows :

> "Since reading this paper I have carefully observed three other cases. In two the point of pain shown by pressure with one finger was two inches and in the other an inch and seven-eighths from the anterior spine

George Washington University
Medical School Washington D C.

ALEC HORWITZ

CHRONIC SYSTEMIC LUPUS ERYTHEMATOSUS

SIR,—Your valuable leading article of April 16 prompts me to report 2 cases I have seen recently

A woman of 45 was admitted to hospital in November 1953 with pneumonia. She had had four attacks and a rheumatoid arthritis during the previous six years. She was found to have bilateral basal bronchopneumonia a rheumatoid form of arthritis, enlarged glands in the right axilla and sclerodermia of the hands Hb was 48% The serum albumin/globulin ratio was reversed and L.E cells were found in the blood smear Pyrexia persisted for weeks despite treatment with antibiotics. There was an immediate remarkable response to corticotrophin. Pyrexia ceased and expectoration of sputum stopped with astonishing rapidity This patient was discharged on 50 mg. of cortisone daily but later the kidneys were involved with albuminuria and uræmia and she died about a year after discharge

A man of 49 was admitted to hospital in June 1954 following five to six weeks of diarrhœa, with blood and mucus in the stools, and painful swelling of both legs Similar attacks of diarrhœa and pain and swelling in the legs had occurred at intervals for the past five years. He had had many attacks of episcleritis in the previous ten years. He had low fever episcleritis in the left eye cellulitis of the left leg and an anal fissure A barium enema showed appearances typical of ulcerative colitis Hb was 75%. Serum proteins were within normal limits. L.E. cells were found in the blood-smear Treatment with corticotrophin was started a month after admission. The pyrexia ceased within a few days and the diarrhœa stopped with astonishing rapidity The anal fissure healed shortly thereafter This man is out and about on 50 mg cortisone daily

These 2 cases represent a chronic form of systemic lupus erythematosus which appears to be commoner than its acute manifestations[1] Both presented without superficial skin lesions or albuminuria The clue to diagnosis in such cases seems to be recognition of the association of recurrent febrile illnesses such as pneumonia pleurisy, pericarditis conjunctivitis colitis &c with involvement of other systems notably the joints and lymph glands. Examination of the blood for L.E cells may be unexpectedly helpful

North Middlesex Hospital
London N 18

D FERRIMAN

CORPORAL PUNISHMENT IN SCHOOL

SIR—The question of corporal punishment in school and the principle underlying it should be decided on the rational ground whether it is favourable or not to the health of children in general As I see it this is a crucial and pressing issue not perhaps especially for doctors but for any society seriously concerned with the health of its children Perhaps therefore you will allow me to make some points on this question

The parent who nags his child to "concentrate who censures him for incontinence or thrashes him for pilfering is in the same boat with the teacher who cuffs his pupil for not attending to the board or for adding 2 and 3 to make 11 They are behaving exactly like the mechanist philosopher who by tradition has explained learning in terms of the law of use and the pain pleasure principle The former was based on the idea that repeated stimulation of a sensory nerve facilitated a muscle response the latter that pain inhibited and pleasure facilitated a muscle response

In the last half century the *Gestalt* scientists have produced an overwhelming mass of evidence against a mechanistic explanation of natural processes. They have established that the behaviour of living organisms is governed by the laws of organisation and they use the word insightful" to characterise the behaviour of all conscious organisms. Let anyone reflect whether a child has ever learned to be generous to control his bladder to solve a problem in mathematics to use crayon, brush, or tool through pain or fear or insightless drill In fact all these abilities are functions of the maturation and differentiation of the brain muscle gland organisation and the insight that depends on them.

That physiological processes like the maintenance of the acid base balance and of the constancy of the internal temperature are organised processes, justifies Cannon's use of the phrase the wisdom of the body Cannon has further shown that when an animal is affected by *any* painful situation it mobilises its energy for muscle action designed to relieve the stress and restore the animal's balance and unity Pain is thus not a deterrent but a positive incitor to action on the part of an organised being like an animal or child It is stress demanding resolution in action.

I consider that sexual tension grows out of" emotional tension in general and it is therefore easy to understand the two way traffic between sexual and any other kind of emotional tension I have known a child in whom masochistic behaviour had been evoked in infancy flee from punishment in school as from mortal danger and I have seen a hysterical reaction provoked in a teen-age girl at the mere witnessing of the punishment of other children. Any mode of education which uses punishment as a tool establishes a sado masochistic relationship between child and parent on the one hand and pupil and teacher on the other which will colour the child's whole life

But further the unremitting punitive tensions in home and in school to which children are subjected in certain areas are in my opinion a decisive factor in the production of serious physical illness. If, as I believe resistance is a condition of energy of the child as a whole then punishment will render him susceptible to illness by lowering his resistance

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[1] McBurney C A) med J 1889 50 676

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[1] Tumulty P A J Amer med Ass 1954 156 947

The analysts maintain that the child can "adapt" by using the punitive tensions of authority to build up his super ego and other internal forces of resistance He will then become a "good" person But he will externalise his "unconscious sense of guilt" and many such individuals are always "looking for something to forbid" and cannot even observe the natural behaviour of children without experiencing an inner compulsion to lay hands on them It is not surprising that analysis is confronted with the paradoxical situation of having to restore to broken lives the unity that they possessed in the beginning

Finally, what moral argument is there on behalf of punishment or the "threat of the withdrawal of love" as an instrument of education? As Kenneth Walker says in his *Sex and Society* "It is a betrayal of every spiritual value we profess to hold in reverence, to use love as a bait or a weapon of coercion"

D Jackson
County Psychiatrist and Director,
Cornwall Child Guidance Service
Perranporth, Cornwall

A VISIT TO KOLTUSHI

Sir,—I found the article by Mr Ruscoe Clarke and Dr Leonard Crome (April 2) most interesting Of interest, too, were the comments of last week of Dr Mungo Douglas in that they represent a distaste for Pavlov's work which is by no means unusual in the British profession

However, one cannot but contrast the meticulous objectivity of the Pavlov school with the doctrinaire disregard of facts shown by Dr Mungo Douglas Instead of criticising the experimental findings, quoted by Mr Clarke and Dr Crome, he asks the rhetorical question "Is it a study likely to provide the kind of future we should all desire ?"

If it can be shown that the great mass of data accumulated by the Pavlov school is all wrong, or if it can be shown that these facts are without relevance to, for example, gastric function, bronchospasm, or, as suggested by Pavlov, schizophrenia, then it is open to Dr Mungo Douglas to prove his case But, in the scientific world at least, generalisations about vital freedom and enslavement cannot be accepted as a substitute for the dispassionate consideration of established facts

Personally I welcome all facts relating to conditioned reflexes since they touch on some very fundamental problems and suggest some interesting possibilities in clinical application

Sheffield C H Foggitt

PSORIASIS SPONDYLITICA

Sir,—Dr Lydon (April 30) asks us to support the unitarian theory of the pathogenesis of the rheumatic diseases This concept has, however, in the past, proved unhelpful in furthering our understanding of these disorders of connective tissue Moreover, as Professor Kellgren has pointed out,[1] just as no sensible person would seriously suggest that all diseases of the nervous system have a single ætiological factor, so it is equally unlikely in the case of the diseases of the supporting structures It is probable that research into the fundamental cause or causes of the rheumatic diseases will be easier once a greater knowledge of the normal anatomy and physiology of connective tissue and of the various clinicopathological entities which we call the rheumatic diseases has been acquired

As the expression of a useful piece of clinical observation, I, for one welcome the term "psoriasis spondylitica" used by Dr Fletcher and Dr Rose (April 2)

One other point arises from Dr Lydon's letter he is incorrect in regarding the arthritis of Reiter's disease as indistinguishable from rheumatoid arthritis—it differs from it in the joint "pattern" and in its course Reiter's arthritis predominantly affects the joints of the lower limbs, especially the knees and the ankles, it is also much more benign, and seldom leaves any permanent crippling deformities except in the feet

London W 1 J F Buchan

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[1] Kellgren J H *Brit med J* 1952, i 1093

NON-PROGRESSIVE BREAST CANCERS

Sir,—Further evidence of the common occurrence of non-progressive, non lethal lesions, in general indistinguishable microscopically from lethal breast cancer, appears to be requisite for a fuller realisation or acceptance of the limitations of treatment Such evidence is obvious, I think, in the data of two series of cases cited previously[1] and other related data In one series, stage 1 (i e, confined to breast) constituted 50%, the 5 year survival-rate in the whole series was over 60%, and in the stage 1 cases it was 85 6% In the other series the respective figures were 16%, 43%, and 81% Consideration of all factors left no reasonable alternative to the deduction that the majority of stage 1 cancers in the first series were non-progressive lesions, and that they accounted, though not necessarily exclusively, for the unusually high 5 year survival rate for the whole series and largely accounted for the high 85 6% rate in the stage 1 cases The near equality of 85 6% and 81%, and the similarity of both with the rates usually obtained in stage-1 cases, point to similarity in the material providing these rates In other words, as the majority of the stage 1 forming 50% in the one series appeared to be non progressive lesions, it seems a reasonable deduction from the similarity of the survival-rates that the majority of stage-1 cancers in most series are similarly non progressive lesions The high proportion of non progressive lesions in the stage-1 cases could then explain, reasonably and consistently, the high survival rates in the latter In contrast to the contention that stage 1 lesions are progressive lethal cancers in an early and curable stage of development, this explanation is fully compatible with the persistence of level trends in age specific mortality in spite of an increase in stage 1 in the treated cases, compatible, too, with the wide variations in reported survival-rates in different series, and with frequencies of stage 1 and of grade 1 as found at different durations.

This does not imply that all the difficulties of differentiation are confined to stage 1 cases The wide difference in survival time even in well advanced cancer, both untreated and treated, reflects wide difference in the degree of malignancy in such cases That difference is not fully revealed even with grading of tumours by microscopy Lewison, in the Halsted Clinic, carefully re-examined sections from the tumours of patients who had survived ten years or more but found nothing on which to prognosticate the long survival[2] Morley et al found approximately the same five and ten year survival rates in *cases clinically stage 1 but pathologically* stage 2 (axillary involvement) as in cases clinically stage 1 but pathologically stage 1 The rates lay between those in stage 1 and those in stage 2 (clinically and pathologically) While the near equality of the survival rates in the two groups could be due to chance, it may indicate a degree of distribution of malignancy somewhat representative of such cases as those described An unidentified increase in such *clinically stage 1 but pathologically stage 2* cases in series treated in successive quinquennial periods *could thus* be a factor in the progressive increase in survival rates in the cases with *axillary involvement as reported* by several clinics[3]

As Smithers et al. have emphasised[4] survival rates are influenced by factors other than diagnosis and differentiation, such as difference in selection of cases after diagnosis, in staging criteria and their application, in detection of lymphatic involvement, in follow up, in calculation of survival rates, &c. However, when, in fifteen series of *different* time or place and for which the necessary data were available, the 5 year survivals of stage 1 were deducted from the over all 5-year survivals, the net 5 year survival rates then ranged from about 10% to about 30%, with the majority close to 20% They thus approximated to what might be found in untreated

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1 *Lancet* 1954, i, 251
2 *J Amer med Ass* 1953, 153, 905
3 *Brit med J* 1953 ii, 787
4 *Brit J Radiol* 1952, suppl no 4

lethal cancers. This suggests that the content of non progressive lesions, as stage-1 cancers, is the most potent factor distorting survival rates and suggests also that the varying inclusion of such lesions accounts for most of the difference between survival rates of untreated and treated cases as well as between the rates of treated cases

These points are fully consistent with evidence previously reviewed, fully compatible, too with the findings of Murley et al. that all different treatments gave the same survival rates,[3] and also with the findings of Small and Dutton that some patients with treated breast cancer die at normal rates and others die at increased rates that "mortality in cancers is a constant process, little affected by treatment" and that 'it is doubtful if many more persons are cured by radical mastectomy than by other forms of treatment.'[5] The deductions or suggestions here really go little beyond what is already well recognised and is implicit in all the efforts that are being made to find a sounder basis for prognosis than microscopy provides.

Department of Epidemiology
and Biometrics,
School of Hygiene
University of Toronto

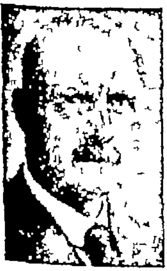
N E McKINNON

Obituary

HUGH ALLAN MACEWEN
O B E. M.B Glasg D.P H. F R.S.E.

Dr Hugh Macewen a former senior medical officer of the Ministry of Health, died at his home at Innellan, Argyllshire, on April 17

He was a son of Sir William Macewen professor of surgery in Glasgow University He entered the same university and graduated M.B in 1905 He early decided to specialise in public health, taking the D P H of Cambridge and of the London conjoint board in the following year He gained experience as assistant M.O H of Cumberland and M.O H of Fife and Kinross, and later visited the United States, where he was lecturer on hygiene at Cooper Medical College, San Francisco To this period belong his excellent manual on *Food Inspection* his account of *The Public Milk Supply* and his investigations into conveyance of whooping-cough from man to animals by direct experiment


Elliott & Fry

When Macewen was appointed a medical inspector of the Local Government Board Sir Arthur Newsholme then the medical officer of the board lost no time in employing him in important investigations He worked at first in the foods branch and then chiefly directed his attention to epidemiology His *Report on the Prevalence of Poliomyelitis in Certain Districts of Lancashire and Westmorland* (1914) confirmed the views of Wickman Reece, and others that the disease was spread by contact infection

During the first world war Macewen acted as one of the liaison officers between the War Office and the board in the inspection of military camps and hospitals in England and Wales and he was appointed O B E for his services. He became a medical officer of the Ministry of Health in 1919 From then onwards he was chiefly employed in medical administrative work at headquarters. His immediate chief was Colonel R J Reece the epidemiologist, for whom he had a warm friendship Macewen's abilities soon marked him out for promotion and a few years after the establishment of the Ministry he became senior medical officer of the branch of sanitary administration in relation to infectious disease With the passing of the Local Government Act in 1929 the Ministry became concerned with the new municipal hospitals and their efficiency and Macewen was appointed the senior medical officer of the branch which dealt with public health surveys, hospitals, and public-assistance medical services. This work he directed with his usual thoroughness and success. He was in charge of the special investigation into maternal mortality which was published as a white-paper by the Ministry of Health in 1937 In this inquiry his wife, Dr Barbara Cunningham O B E., took an important share. In the early years of the second world war he was in charge of the regional medical organisation, and it was once said that even the evacuation scheme for expectant mothers could not remove the smile from his face

In 1941 Macewen retired from the Ministry but not from medical practice He became medical superintendent of Ballochmyle Hospital in Ayrshire and acted for a time as M.O H of Ulverston rural and urban district in North Lancashire

As a senior medical officer at the Ministry in the 'twenties and thirties he came into close contact with the medical officers of the large local authorities and as the years went by he came to be more and more trusted by them. Many became his personal friends and one of them, W M F, writes 'Macewen showed his devotion to the cause of public health in everything he undertook. Despite the clinical atmosphere in which he was brought up, as the son of Sir William Macewen, he was convinced of the supreme importance of preventive medicine Before he began his long and successful career at the Local Government Board and at the Ministry of Health he was a medical officer of health and after his retirement, he became—temporarily—a medical officer of health again. To him and his colleagues at the Ministry we owe the rapid development of the personal health and hospital services during the twenty-one years between the first and second world wars. He possessed to an unusual degree the characteristic of selflessness Though he rose to a senior position at the Ministry, it was impossible to detect in him any signs of overweening ambition. Incapable of jealousy for himself he was jealous of the reputation of the English public health service'

A. S MacN writes Hugh Macewen was a man whose life and work were dominated by high ideals, and his sense of duty and devotion to the public weal never wavered He was serious in disposition except on social occasions when he would unbend and reveal a sense of humour He retained his Scottish accent was outspoken in his beliefs and while just and considerate to his medical officers, demanded and obtained the best from them Much of his valuable work for the Local Government Board and the Ministry of Health is to be found in official files reports and blue-books, and in all he did he worthily maintained the high standards and traditions of the central health department"

A colleague at the Ministry of Health writes Around 1930 a number of medical officers entering the Ministry were lucky in having Hugh Macewen for their chief and mentor The formidable exterior soon revealed beneath it a real kindness, a devotion to duty and a passion for accuracy which would never tolerate slapdash work. Verify your references—in the widest sense—might have been his watchword The department lost something of the old traditions and standards of the Local Government Board when he left, though he was able to do excellent work in Scotland both during and after the war He finished a fine life beside his beloved Clyde

HORACE BRYDEN HILL
M.B. Lond M R.C.P

Dr Horace Hill, medical superintendent of Laverstock House Salisbury who died on April 25 at the age of 76 was a man of considerable versatility

After qualifying from St Bartholomew's Hospital in 1901 he held house-appointments at Barts and at Huntingdon County Hospital In 1907 he took the M B Lond., and about this time he joined the Royal Navy and became a member of the staff of the Royal Naval Hospital at Haslar He had always been an all round athlete: an international hockey player and a member of the United Services cricket XI he also took a keen interest in boxing and played water polo This background led to his appointment to the staff of the Naval school for physical training at Portsmouth and

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5 J Amer med Ass 1955 157 216

later he became instructor in physical training at the Royal Naval College, Osborne In 1911 he took the M R C P

During the 1914–18 war he served as a medical officer in H M S *Highflyer* He was made knight in the Order of St John of Jerusalem for his reorganisation of the training and service conditions of the Royal Naval Auxiliary Sick Berth Staff Reserve He also collaborated with Naval officers in an investigation of the best method of applying discipline in the Royal Navy He was made a chevalier of the Order of the Crown of Italy for his work in the Messina earthquake

After the war he left the Navy and settled in practice in Harley Street, joining the staff of the Royal Chest Hospital, City Road He was a vice-president of the Medical Defence Union In 1930 he published a handbook for students on *Electrocardiography* In 1936 he became medical superintendent at Laverstock House His later publications reflected his responsibilities and interests in this new appointment In his brochure in the *Public Attitude towards Mental Disease* (1939) he pointed out how desirable it was that relatives should not delay in seeking early treatment for a patient He also published a useful little book on safeguards in certifying those of unsound mind, and a more formal treatise on *Histamine and Insulin Treatment of Schizophrenia* (1940)

He was no mean painter, and some of his paintings hang in the Royal Fowey Yacht Club where he used to spend much of his leisure His widow survives him

DAVID WINN HOODLESS

O B E, B Sc Lond, L M S S A

WHEN Dr Hoodless was appointed the first principal of the Central Medical School in Fiji in 1929, he was already known, loved, and respected in the Pacific, for he had spent almost twenty years in the Colony as a schoolmaster and later as its director of education

Though his father was an engineer Hoodless came of farming stock He was born in 1887 in a small village in Nottinghamshire, and was educated at Sheffield and at King's College, London, where he gained a gold medal for mathematics, graduating B SC with honours in 1910 His first post as a teacher was in the training ship H M S *Worcester*, where he specialised in mathematics and navigation Two years later he went to Fiji as headmaster of a school for native boys, and later of the Queen Victoria School at Suva Through his work he came into close contact with the Fijian people, and his wish to serve them turned his thoughts to medicine In 1919 he came to England for two years to study at Charing Cross Hospital In 1921 he returned to the Pacific as inspector of schools in Fiji, and the following year he was appointed director of education During the five years that he held this post he established five new provincial schools to serve the Indian as well as the Fijian communities and started a scheme for recruiting teachers from New Zealand Such was his determination that he returned to England in 1928 to continue his medical studies, but illness prevented him from taking his finals in 1929 Despite his lack of formal medical qualifications he was wisely appointed the first principal of the Central Medical School When he qualified in 1935 he also took the diploma of tropical medicine

Hoodless did his task in Fiji so well that he was sent to inspect medical schools in Africa, but when the war broke out in 1939 he was recalled as he was indispensable to the Fijian government On his retirement in 1947 he was appointed O B.E He was an associate of King's College In 1953 he became correspondent to *The Times* in Fiji

P M-B writes "The name of Hoodless was one to conjure with in the Pacific He probably did more for medicine and education in Fiji than almost any other man He was the moving force behind the Central Medical School for Polynesians in Suva, and it must have been a great satisfaction to him when two years ago the Queen opened the fine hostel for Polynesians and the ancillary teaching blocks at the school An even greater satisfaction to him was the renown which the graduates of his school won from so many quarters during the late war Many of the Allies, mostly the Americans, were amazed at the knowledge and efficiency shown on many a lonely Pacific atoll by the Polynesian doctors who had been educated in Suva It was the greatest compliment to him that the American government for the island of Guam and the New Guinea government sent their quota of medical students to Suva Throughout the myriad islands of the Pacific he will be mourned as the guide, philosopher, and friend of the Polynesians, for he not only taught but guided and advised them as the ideal leader of their youth "

Dr Hoodless married in 1923 Miss Hilda Adlington, and there is a daughter of the marriage He was on holiday in this country with his wife when he was taken ill at Cambridge He died on April 15

Dr EGBERT MORLAND

S T writes Egbert Morland was a connoisseur of " obits " Not for him the list of dates and appointments culled from the reference books Every obit must stand on its own merits To write dully about the dull was a sin against the craft of journalism The ethic of happy curiosity, which he professed, made him certain that no life could be so barren as to yield nothing of interest, and it was the thing of interest alone which was worth recording But a good obit must not only interest, it must entertain, amuse, or edify It must tell the truth without unduly offending the relatives It must please friends and pacify enemies It must follow no logical pattern, but must blend fact and interpretation into a whole, having an artistic integrity of its own And if, on reading it, our eyes are filled with that divine mixture of laughter and tears, then it may be said to have succeeded

Egbert's attitude to obits followed from his rational Christian view of death Dying might be very unpleasant, but death was a brief moment of transition only and the gateway to another " awfully big adventure " He saw no reason to doubt the spiritual validity of Christ's promised immortality So when those we know or love come to die, selfish sorrow at our loss should deliberately be replaced by joy at their good fortune For Egbert, the conventional condolences and the trappings of mortality were a source of endless delight and amusement

I think Egbert was a Benthamite, a pragmatic utilitarian, to whom happiness was very important indeed. He wanted everybody to be happy, and saw no reason why he should not begin with himself

Despite an occasional witticism at the expense of reformers, he was a reformer himself. He was seeking ever to make the world happier, wiser, and more amusing. He was not always sure of the precise course to follow, but he turned this multivalence to positive advantage He would back people rather than plans Having picked his men or women, he would test them and try them with every devious tortuosity he could devise If they still came up smiling, or at least came up, he would give them their head At times, indeed, his trust was almost alarming So we of his staff were able to become once again " those sharp *Lancet* fellows " who had fought the good fight a hundred years before

Arrogance as a cloak for ignorance he would not tolerate Indeed the puncture of pomposity was a favourite occupation There was no subject on which he was ashamed to confess that he did not know, and he expected a like humility in others He had no patience with the establishment of a committee as an excuse for inaction and his gentle ruthlessness was often an unpleasant surprise to the " No " men of his day

It would be incorrect to say that the truth was not in him But sometimes it took a lot of finding " Always remember," he told me, " that in journalism interest is more important than accuracy " He held the view that the only purpose of writing was to be read If this failed, then the whole thing became a sterile intellectual exercise For the same reason, he loved the stimulating or provocative headline, the carminative which tempted the lazy appetite into operation The right place for the purely descriptive heading was the abstracting journal

Egbert's insight into his tortuosity was complete " Whether I have continued to edit *The Lancet* or become an inmate of Brixton has rested upon a knife-edge A single tiny genetic alteration and the coin might have come down the other way I hope I am enough of a knave not to be a fool "

As the years rolled by, his obliquities became more blique and the knight s moves of his mind took on an ver more fanciful pattern "I cannot solve your roblems, my dear fellow at best, and even this is nprobable, I may perhaps enable you to solve them r yourself' We were talking under a mighty tree in n Aylesbury garden and I left him with none of my onflicts resolved Yet over the months they melted way as perhaps he intended they should. Years before, hen I had been tortured by doubts he had joyously ut me on the right road when he finally saw he saw ith great clarity

Dear Egbert to have worked for you and with ou was a joy which time dims not at all To skip and icnic again with you and Mary in the Elysian Fields eyond the Chilterns robs death of its last remaining ting

E M C writes Your obituary notice of Dr Morland gives a vivid picture of his many sidedness I knew him or many years, but he still had a few surprises up his leeve and of course lots for the unwary who thought him merely eccentric or affected We once had the great joy of a holiday shared with him his wife and amily, and several young relatives. Led by him, the younger end of the party set off over the Gross Glockner pass to spend the night in the hut and go on to see the sunrise By then we were well acclimatised to the sun but I had had little experience of summer sun off the snow and by the evening my face was a mess with sunburn Next day after one look at it, Egbert said quietly, You and I are going to walk home by the valley, and leave the young ones to go over the top This was a great disappointment, but I couldn t question his judgment for I knew he was right. What I did not know was what a treat was in store, for his knowledge of Alpines was encyclopædic. I shall never forget that walk, taking it easy and stopping to look at first one and then the next little masterpiece, held out for me to see or just lifted up from the edge of the snow He felt a little guilty not to have warned me about the sun the day before, but, characteristically, it was the plants with which he was tender

Appointments

ANNELS, E. H., M.B. Lpool D P H deputy county M O Flintshire
KOHN JOACHIM, Med Dipl Lwow D C P consultant in pathology Queen Mary s Hospital Roehampton
MORGAN, D W, M.C. M.B Lond, D P.M whole time senior asst. psychiatrist, Mapperley Hospital Nottingham.
RALPH, L. L. M.B Sheff. D.M R.D part-time consultant radiologist, Chesterfield and Mansfield groups of hospitals
SALFIELD D J, M D Düsseldorf D.P.M whole time children s psychiatrist, Derbyshire county council

North East Metropolitan Regional Hospital Board:

ARNOTT D C. M B Lond., D PHYS. MED D C H part time consultant physician in physical medicine Queen Mary's Hospital for the East End and St Mary's Hospital Plaistow
FOXELL, A. W H. M B Lond consultant pathologist group laboratory, Mile End Hospital
GRUNSBERGER, GEORGE M D Basle D.L O part time consultant E.N T surgeon, Queen Mary's Hospital for the East End
LAVE, RICHARD, M B. Lpool D.M R D part time consultant radiologist St. Leonard s Hospital

Appointed Factory Doctors:

HUGHES F G, M B, N U I Tuxford, Nottingham
MCCALLUM E. L R. M D Toronto Richmond York.
RHYS-DAVIES N C. M R.C.S I Milborne Port Somerset.
WADE O T, M.R.C.S Radcliffe Nottingham.
WILSON A H L. M B Glasg New Abbey Kirkcudbright

Colonial Appointments:

BUTLER, G C., M.B N U I D.P H : senior M.O sleeping-sickness service northern region Nigeria
CHAMBERS, H D M D Aberd : senior M.O , Jamaica.
CUMMIR J R., M.R.C.S pathologist, Sierra Leone
FRANKS I I M R.C.S. L.O.M.S specialist officer (ophthalmologist) Federation of Malaya.
FERN G C., M B Lond F.R.C.S : M O (grade B) Trinidad
JONES D J M.B. Wales : M.O., Federation of Nigeria.
RITCHIE, JEAN K., B.M Oxfd M.R.C.P D M.R.T : radiologist Singapore
SCHURER, W., M.D M.O Gold Coast
THOMAS M.O L.R.C.P I : M.O., Sierra Leone

Births, Marriages, and Deaths

DEATHS

ANNAND —On May 6 at 7 St. Andrew's Road Coventry William Fraser Annand, M.D. Lond., aged 75

Diary of the Week

MAY 15 TO 21

Monday, 16th

UNIVERSITY COLLEGE, Gower Street W C.1
4 45 P.M. Prof E L Smith (Utah) Mode of Action of Proteolytic Enzymes (Second of three lectures)
UNIVERSITY OF ST ANDREWS Queen s College Dundee
5 P.M. Dr R Heim de Balsac (Paris) Vascular Factor in the Radiology of the Lung fields

Tuesday 17th

UNIVERSITY COLLEGE
5 15 P.M Dr J D N Nabarro Adrenal Cortex and Renal Function (Cushny lecture)
ROYAL SOCIETY OF MEDICINE
3 30 P M (London School of Hygiene and Tropical Medicine Keppel Street W C 1) *Epidemiology and Preventive Medicine* Meeting to celebrate centenary of publication of Snow s work on cholera
4 30 P M (1 Wimpole Street, W 1) *Proctology* Mr Harold Edwards, Dr E N C McAmmond (Vancouver) Dr Raymond W McNealy (Chicago) Mr Stanley Aylett Diverticulitis of the Colon
WRIGHT-FLEMING INSTITUTE OF MICROBIOLOGY St Mary's Hospital Medical School, Paddington W 2
5 P.M. Mr A T R. Mattick, PH D Lactobacilli and some Streptococci
INSTITUTE OF DERMATOLOGY St. John s Hospital Lisle Street, W C 2
5 30 P.M. Dr S C. Gold Drug Eruptions

Wednesday, 18th

POSTGRADUATE MEDICAL SCHOOL OF LONDON, Ducane Road W 12
2 P.M Prof G Payling Wright General Pathology of Tuberculosis. (Last of three lectures)
ROYAL SOCIETY OF MEDICINE
8.30 P M *General Practice* Lady Barnett M B.: T V and the General Public.
INSTITUTE OF DERMATOLOGY
5.30 P M Dr J O Oliver Prevention of Hospital Infection
SOUTH WEST LONDON MEDICAL SOCIETY
8.30 P.M. (Bolingbroke Hospital Wandsworth Common S W 11) Mr A Dickson Wright Varicose Veins, (Bolingbroke lecture)
HYPNOTHERAPY GROUP
8 P.M (1 Wimpole Street, W 1) Dr A Fry, Dr N S. Shorrard Dr R. M. Harrison Dr R B J Ridge Hypnotherapy in General Practice.

Thursday, 19th

ROYAL COLLEGE OF SURGEONS OF ENGLAND Lincoln s Inn Fields W C.2
5 P.M. Mr H R. S Harley Subphrenic Abscess
POSTGRADUATE MEDICAL SCHOOL OF LONDON
4 P.M Dr C M. Fletcher Atmospheric Pollution and Disease
UNIVERSITY COLLEGE
4 45 P.M Professor Smith Mode of Action of Proteolytic Enzymes. (Last of three lectures.)
BRITISH INSTITUTE OF RADIOLOGY 32 Welbeck Street W 1
8.30 P.M Mr J A. C Fleming Position and Scientific Rôle of the Institute (Presidential address)
ROYAL SOCIETY OF TROPICAL MEDICINE AND HYGIENE, 26 Portland Place W 1
7.30 P.M Prof A Corradetti Studies on Comparative Pathology and Immunology in Mammal and Bird Plasmodium Infections
WEST LONDON MEDICO-CHIRURGICAL SOCIETY
8 30 P.M. (Royal College of Physicians Pall Mall East S W 1) Sir Charles Dodds F.R.S Renaissance of Treatment (Cavendish lecture)
HONYMAN GILLESPIE LECTURES
5 P M (University New Buildings Teviot Place Edinburgh 8) Dr J H Wright : Unilateral Renal Hypertension
UNIVERSITY OF ST ANDREWS, Medical School Small s Wynd Dundee
5 P M Prof Alan Kekwick Obesity

Friday, 20th

UNIVERSITY OF LONDON
5 P.M (St Thomas s Hospital Medical School S.E.1) Prof V Erspamer (Bari) Biological Significance of 5 hydroxytryptamine and Related Substances
POSTGRADUATE MEDICAL SCHOOL OF LONDON
2 P.M Mr A L d Abreu Surgery of Congenital Heart-disease
4 P.M Dr Ian Douglas Wilson Words without End
UNIVERSITY COLLEGE
5 15 P M Dr Harry Harris : Genetic Aspects of Tubular Function (Cushny lecture)
ST MARY S HOSPITAL MEDICAL SCHOOL, W 2
5 P.M Dr F S W Brimblecombe : Lactation and Breast-feeding
FACULTY OF RADIOLOGISTS 45 Lincoln s Inn Fields W C 2
4 30 P M Dr S Whately Davidson Anomalies of the Respiratory System (Skinner lecture)
OSLER CLUB
8 P.M. (Royal Army Medical College Millbank, S W 1) Sir Gordon Gordon Taylor Reminiscences of Some Famous Surgeons of the 1914–18 War
UNIVERSITY OF ST ANDREWS Queen s College, Dundee
2.30 P M Dr J H Wright Dr R. W D Turner Prof Robert Walmsley Dr K. G Lowe : Pulmonary Stenosis as an Isolated Lesion and with associated Atrial Septal Defect (Fallot s trilogy)

Notes and News

HEALTH CENTRES AT YORK AND STRANRAER

WITHIN the past month two new health centres have been opened—at York and Stranraer

Performing the ceremony at York on April 14, Sir John Charles, chief medical officer of the Ministry of Health, declared that there was nothing so inspiring, so apt to promote smooth and efficient performance, as the outward and visible signs of bricks and mortar—such a sign as the new centre The centre is in the middle of a large post war housing estate and it will serve a population of about 25,000 In the first place, it will provide maternity and child welfare, health visiting, school nursing, and dental services, but the building has been designed in such a way that an extra wing of consulting rooms for general practitioners can readily be added later Alternatively, general practitioners may rent some of the existing accommodation, and discussions on this question are in hand The centre has been planned so that different kinds of patients are in independent units but they can all be easily supervised from the central administration offices The cost of the present building was £13,000

Stranraer's health centre is the second to be newly built in Scotland (the other is at Sighthill in Edinburgh [1]), and the first to be built adjoining or connected to an existing hospital It contains five consulting suites for the general practitioners of Stranraer, who have a total of 13,200 people on their N.H S lists In another wing there are three rooms and a dental workshop for local authority services, and the local authority will share another four rooms with the board of management responsible for the adjoining Garrick Hospital In addition the hospital has for its own use a changing room, a plaster room, and rooms for an X-ray unit The cost was about £33,000, of which the hospital authority will contribute some £12,000 The centre was opened on May 6 by Mr H R Smith, secretary of the Department of Health for Scotland

University of Oxford

On April 28 the following degrees were conferred

D M—Zelda M Hall Constance L Simpson
D Sc—W Ritchie Russell

University of Glasgow

On April 30 the following degrees were conferred

M D—M C Macleod (honours), R C MacLeod.
Ph D—T C D Whiteside

Royal College of Physicians of Edinburgh

At a meeting of the College held on May 3, with Sir Stanley Davidson, the president, in the chair, the following were elected to the membership

J M Johnston H R Harris T M Desai L Molk M. B Azami R H Aldons S K Mazumdar, D O Lewis, D A Kerfoot E N A Magid, J Richmond, E Schiller W G Smith S S Levin E S Nash J R. Shah B C Syam I J Pinto R C Parikh N H Brooke S C Jain, B Cowan, R. H C Rischbieth W H Wolfenden J C Pond M Wakefield, G D Campbell, B C Paton, M A Kibel

Hunterian Society

Mr A Dickson Wright has been elected president of this society for 1955–56

Royal Society of Tropical Medicine and Hygiene

The Chalmers medal for 1955 has been awarded to Dr W E Kershaw, lecturer in medical parasitology, Liverpool School of Tropical Medicine

N A P T Travelling Fellowship

The Scottish branch of the National Association for the Prevention of Tuberculosis offers a travelling fellowship (£250), for postgraduate study abroad, to a doctor working in Scotland on tuberculosis Applications should be sent not later than July 15 to the Scottish secretary, N A P T, 65, Castle Street, Edinburgh, 2

British Society for Research in Ageing

This society will hold a symposium on Thursday, June 9, at 2 P.M, at 41, Portland Place, London, W 1, on Endocrinology and Ageing Prof G R Cameron, F R S, will be in the chair The speakers will include V Korenchevsky (London), J A Loraine (Edinburgh), P L Krohn (Birmingham), and P J Thung, L Boot, and O Mühlbock (Amsterdam) Further information may be had from the hon secretary, Mr G H. Bourne D.SC, London Hospital Medical College, Turner Street, E 1

Sydney Body Medal

This medal has been awarded to Dr L Gordon Hopkins "for his unsurpassed services to medicine during fifty years in Southend."

Medical Records Exhibition

This exhibition will be held at the Bonnington Hotel, Southampton Row, London, W C 1, from 10 A.M to 6 P.M on Saturday, May 21 At 11 A M Dr N M Goodman will give a lecture on Statistics and Records of Cancer The exhibition has been organised by the Association of Medical Records Officers to help hospital staffs to deal with problems of indexing, correspondence, outpatient waiting, admission and discharge procedure, and storage of records

International Society for Human and Animal Mycology

Last year, at the 8th International Congress of Botany, this society was founded to bring together those interested in the study of fungi living on humans and animals The president is P Redaelli (Milan) and one of the vice-presidents is G T Ainsworth (Exeter) Further particulars may be had from Prof R Vanbreuseghem, Institute of Tropical Medicine, 155, rue Nationale, Antwerp, Belgium.

Hospital for Tuberculosis in Malaya

Dr M R J Snelling, chest physician at the King Edward VII Sanatorium, Midhurst, has been appointed the first medical superintendent to the Lady Templer Hospital for Tuberculosis at Kuala Lumpur This new hospital, which has 250 beds, is to be run on similar lines to those of the King Edward VII Sanatorium. A thoracic surgeon and a team are shortly to join Dr Snelling, and Australia is sending 28 nursing sisters

French Prize for Medical Film

At the fourth distribution by the *Presse Médicale* of prizes for medical films the prize for the best foreign entry was awarded to C E Engel (London) for his film on *Mitral valvulotomy for mitral stenosis* Honourable mention was given to the film by P Hansell (London) on *Grafting on the cornea* Applications for next year's competition will be received up to the end of next February, addressed to the *Presse Médicale*, 120 Boulevard Saint Germain, Paris VI

Nursing Times

The golden jubilee of the *Nursing Times* was marked by a luncheon in London on May 6, under the chairmanship of Mr Daniel Macmillan Sir Harold Boldero recalled that only in the past half-century had nursing become fully established as a profession landmarks in this period included the foundation of the College of Nursing in 1916, the Registration Act of 1919, and the adoption by the college of the *Nursing Times* as its official journal in 1926 He went on to refer with regret to the fragmentation of medicine, and wondered whether the same sort of thing was happening in nursing Did those engaged in teaching nursing—who seemed to spend all their time on this task—go into the wards and see what was being done there? Did district nurses go into the hospitals? The medical curriculum was admittedly overloaded, and he asked whether the nursing curriculum was similarly overloaded or (which came to the same thing) there was insufficient time in which to teach everything included in the curriculum. Miss M. L Wenger, editor of the *Nursing Times*, spoke of some of that journal's activities Recently these had included the encouragement of recruitment to the mental hospitals and the offer of a bursary to enable a nurse to spend a year in the study of journalism, for they believed that nurses should be able to describe the results of their work. Dame Enid Russell Smith enunciated five aims for a professional journal First, it should advance professional knowledge (of course in language understandable to no layman) secondly, it should present professional political issues without bias, bitterness, or personalities, thirdly, it should put the work and aims of the profession in the setting of the fuller scheme of things (the margin between proper professional pride and arrogance was narrow), fourthly, it should set a high standard of professional ethics and support the best traditions (thus acting as the profession's memory); and fifthly, it should encourage the pioneering spirit, so that no reader, after studying any issue of the journal, could feel any self satisfaction at all The *Nursing Times* had succeeded in each of these aims Finally Miss S C Bovill spoke with pleasure of the association between the Royal College of Nursing, of which she is president, and the *Nursing Times*

A draft British standard for gas-cylinder trolleys has been issued by the British Standards Institution Comments should be sent to the institution 2, Park Street London W 1, before June 7

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[1] See *Lancet* 1953 i, 1038

THE CLINICIAN AND
E PROBLEM OF MULTIPLE SCLEROSIS*

Douglas McAlpine
M.D Glasg F R C P

ICIAN IN CHARGE OF DEPARTMENT FOR NERVOUS DISEASES, DLESEX HOSPITAL, LONDON PHYSICIAN MAIDA VALE HOSPITAL FOR NERVOUS DISEASES

DURING the past quarter of a century there has been a able revival of interest in multiple or disseminated rosis particularly in America In the laboratory the erimental pathologist has evolved a technique by ich an encephalomyelitis can be produced in animals luding the monkey by means of subcutaneous or amuscular injections of brain tissue along with an uvant consisting of heat killed tubercle bacilli. The ults of these experiments have suggested to some ervers that brain tissue may contain a chemical agent ich acts as an antigen producing antibodies that react h constituents of white matter The part played by adjuvant used in these experiments is uncertain

Meanwhile, clinicians have contributed mainly in two ections—first in geographical and racial studies and ondly in attempts to determine more accurately the ure of the disease.

Geographical surveys were undertaken first in Switzer d by Bing and Reese (1926) and subsequently in nmark (Gram 1934) Sweden (Sällström 1942), and ts of the United States of America (Kurland 1952) st of these surveys have suffered from one serious ect—namely that the results have been based either death certificates or on information obtained from eral practitioners. Notable exceptions have been those ently carried out by Allison and Millar (1954) in thern Ireland and by Dr John Sutherland in Northern tland

Allison and Millar personally examined all cases orted to them by general practitioners over a three ar period After discarding 187 cases 700 remained in ich they were satisfied that the diagnosis was either bable or possible Using the census figures of 1951 y were able to arrive at a prevalence rate of 7 0 per 000 after excluding persons under the age of 20 By ermining the geographical distribution by place of et, Allison and Millar found that the disease in rthern Ireland does not affect rural populations more n urban nor did they find any evidence to suggest a al incidence

Dr Sutherland has recently completed a survey of the ease in the Orkney and Shetland Isles the Western es and the mainland counties of Caithness Sutherland ss and Cromarty Inverness, and Nairn I am grateful him for permission to refer to certain of his findings questionnaire was sent to all general practitioners in se regions asking for the names and addresses of all pected cases of multiple sclerosis; replies were received m 93% of practitioners 180 cases were notified of ich 16 were rejected 10 other patients had either ed after the case had been notified or had removed from region these 10 cases were discarded Of the maining cases 127 were classified as probable and as 'possible cases of multiple sclerosis On the is of the 1951 census figures Dr Sutherland found an er-all prevalence rate of 5 5 per 10 000; if possible ses were included the figure rose to 6 7 In the Shetland es the relative figures were 11 3 and 12 0 per 10 000 e highest rate yet recorded in Great Britain

In the Northern Ireland and Northern Scotland rveys a significant familial incidence was found to hich I shall refer later

The results of these surveys justify the hope that similar field studies of multiple sclerosis in Great Britain will be encouraged, particularly in areas with a reputedly high prevalence rate

Other contributions made by clinicians in recent years include studies of the course of the disease and its prognosis In the past estimates of its duration were usually based on fatal cases. A notable exception was Byrom Bramwell's (1917) follow up of a series of cases over a period of twenty years However, the main credit for introducing some order into this subject must go to Ragnar Müller (1949) whose conclusions are of particular value because of the size of his material and his application of the statistical method His results and those of other workers including Allison (1950) have shown that the outlook for the patient with multiple sclerosis is considerably better than was formerly supposed

These outstanding contributions must not blind us to the fact that other aspects of the natural history of the disease as well as its symptomatology have been largely neglected in recent years My primary purpose here is to indicate the further value of these two lines of study

Aspects of the Natural History

The Familial Incidence

Preoccupation with the hereditary forms of cerebellar and paraplegic disorder may be the main reason for the long delay in the recognition of a small but significant familial incidence in this disease It was the appearance of Curtius's paper in 1933 that stimulated interest in this subject. He found a familial incidence in 6 4% of 106 cases observed in Bonn and Heidelberg (Curtius 1933 Curtius and Speer 1937) Since no case of multiple sclerosis was detected in a control population he concluded that the incidence of secondary cases in the families of multiple sclerosis patients was considerably raised when compared with a control population Since 8 positive family histories were obtained in a series of 142 cases reported from the Middlesex Hospital in 1946 an additional series was investigated with Pratt and Compston (1951) In a total of 310 cases the familial incidence was 6·5% In the Northern Ireland survey the figure was 6 58% Millar and Allison were the first to compare the expected risk in siblings of patients with multiple sclerosis with the rate in a control population studied in the same area and at the same time They estimated the risk to be about ten times greater in siblings of patients than in the control population and agreed with our view that the excess risk is not due to a common environment or to infection but to a genetically determined predisposition In the Northern Scotland survey there were 12 families with more than one case of multiple sclerosis an incidence of 9·4% This figure errs on the conservative side since in 12 other families there was a positive history but as the diagnosis could not be satisfactorily established in the secondary cases they were excluded Dr Sutherland rejected a diagnosis of multiple sclerosis in three brothers living in the Island of Lewis affected by a progressive spastic paraplegia preferring to regard it as a purely hereditary condition In the Orkney and Shetland Isles the familial incidence exceeded 10% Parental consanguinity seemed a possible explanation for this high figure but the incidence proved to be comparatively low Dr Sutherland's observations which cover racial dietetic and other factors may throw further light on the relative parts played by heredity and environment in this disease

Precipitating and Aggravating Factors

At the end of the last century and the beginning of the present one there are many references in the literature especially German to the effect of such factors as infection injury physical exertion exposure to damp and cold emotional upset, and prolonged worry in unmasking

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The Florence Tong lecture delivered before the Association of British Neurologists at Cambridge on March 25 1955

6378

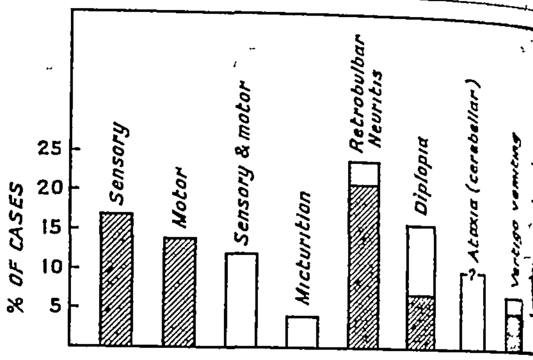
the first symptoms of the disease In 1934 Hoesslin published a monograph devoted to these so called exogenous factors

The criteria necessary to establish a causal relationship between a supposed precipitating factor and the onset of the first symptom of multiple sclerosis or a relapse are (1) a temporal relationship, and (2) a significant incidence of the factor in comparison with a control series The time interval is difficult to fix, and a period of three months which we arbitrarily chose in studying these factors seemed reasonable (McAlpine and Compston 1952) However, if it could be shown that a causal relationship may exist between trauma, for example, and the onset of the disease, it would be necessary to visualise a longer time-interval than three months Turning to the second point, the evidence in the literature is of little value judged by present day statistical standards Bearing this fact in mind I propose to discuss briefly four conditions which appear with sufficient frequency in the immediate past history of these patients as to warrant attention

General health —It is by no means exceptional to find that for days or weeks before the appearance of the first symptoms, or accompanying them, the patient has not felt in his or her usual health, has lacked energy, has tired easily, and in addition may have noticed headache and vague pains in the back or limbs On inquiry these somewhat indefinite symptoms may have coincided with a period of overwork or overstrain, but in other patients no adequate cause can be found Although by no means the rule, these premonitory symptoms deserve further study, since if we understood their meaning they might provide a partial clue to the ætiology of the disease

Infection —This usually takes the form of a cold, a sore throat, or influenza Bramwell obtained the high figure of 14% of infections preceding the onset in 200 cases, and Hoesslin 10 5% in 109 acute cases, which is approximately the figure obtained by Compston and myself in 250 consecutive cases Taking these figures and those in other series into account, it may be said that 10% represents the approximate incidence of some form of infection before the onset. If attention be paid to this question it will be found that not infrequently in an established case of the disease, a relapse may immediately follow an upper respiratory infection

Trauma —The third factor is trauma, whose occasional relationship to the onset of multiple sclerosis has been commented upon by numerous writers (McAlpine and Compston 1952) In our own series of 250 consecutive cases particular care was taken to exclude trauma from a fall due to the disease In the three months preceding the onset there was a history of trauma, including dental extractions but not surgical operations, in 36 patients (14%) as compared with a similar history in 13 patients (5 2%) in a control series of hospital inpatients With regard to the site and degree of trauma, it has been assumed by most writers that the injury must be cranial or spinal and severe in degree (Keschner 1950) Whether the changes set up in the nervous system are primarily vascular or chemical, there seems no reason to exclude the limbs when considering the site of trauma Hoesslin was the first to suggest that there may be a relationship between the site of the trauma and that of the first symptom Of our series of 250 cases, in 22 out of 36 (61%) patients who gave a history of trauma, there appeared to be a correlation between the site of the injury and the part of the body, usually a limb, in which the first symptom appeared We also showed that the relapse rate within the three months following trauma, whether this was accidental or surgical, was significantly greater than the expected relapse-rate during the same period This evidence, of which fuller details are given in our paper, suggests that slight or severe trauma, including an operative procedure, to a limb or any part of the body, may occasionally precipitate the disease or may be the cause of a relapse



Initial symptoms of multiple sclerosis, occuring alone (hatched columns) or in combination, in 309 cases.

Allergic disorders —The incidence of allergic disorders in the past history of patients will naturally depend on the scope of the inquiry In our series we found no significant difference in the remote past history of multiple sclerosis patients as compared with a control group , but in the three months preceding the onset of the disease, and in the subsequent months or years, such a history was obtained in approximately 9%, as compared with an average of 2 8% in a control series.

If mental stress be added to the factors which I have mentioned—namely, a lowered state of general health, trauma, infection, and an accompanying allergic disorder —it may be estimated that one at least of these occurs in a close time relationship to the onset in roughly every other patient, an estimate which probably errs on the conservative side

Features of the Early Symptomatology

There is still no consensus of opinion as to the relative incidence of the initial symptoms It therefore seems worth analysing the notes of the 309 cases finally diagnosed as multiple sclerosis after admission to the Department for Nervous Diseases, the Middlesex Hospital, under myself and my colleague Dr Michael Kremer, over a five year period from January, 1950, to December, 1954 Doubtful cases were excluded By limiting the analysis to inpatients admitted to the same department it was hoped that some degree of uniformity in history taking, methods of investigation, and final diagnosis would be achieved

In constructing the accompanying figure, motor and sensory symptoms associated with brain stem signs have been omitted , so the columns marked " motor " and " sensory " refer to cases in which there was a high probability of one or more plaques in the spinal cord Symptoms rarely met with at the onset, such as an isolated facial palsy, have also been excluded

This analysis emphasises the frequency of a monosymptomatic type of onset, which was seen in nearly two thirds of the cases in this series An isolated retrobulbar neuritis may be expected as the first sign in about one patient in every five , parresthesiæ in one out of every six , and thereafter, in diminishing order of frequency, motor weakness (usually in a lower limb), double vision, vertigo, and vomiting

One of the characteristic and at the same time puzzling features of multiple sclerosis is the extreme variability in the mode of onset and duration of the first symptom At one end of the scale is the so-called apoplectiform onset recognised by Charcot , at the other end is the slow insidious appearance of a paraplegia due to spinal plaques How to explain these two modes of onset on the basis of a common pathological process is one of the many unanswered questions relating to this disease Tr oints, however, should be borne in mind: first the age ncidence differs, an abrupt onset being more common in ounger patients while the slowly progressive form of ne disease mainly occurs in those over the age of 40 nd secondly as in certain other diseases—notably heumatoid arthritis—the individual's reaction to the orbid process can apparently determine the tempo of ne initial symptoms and the subsequent course

ransitory Episodes and Exacerbations

The adjectives "transitory' fleeting or short ved" are often used by writers in describing early ymptoms. The vagueness of these terms leaves the verage reader in some doubt as to their meaning hough he may gain an impression that they indicate a eriod of one or more days. Accordingly serious attention seldom given to attacks of blurred vision double vision iddiness, or pins and needles in a limb lasting a few ours or even minutes. Yet such episodes are not ncommon in the past history of patients presenting ith undoubted signs of the disease

The factors determining the onset of these fleeting arly symptoms deserve further study So far as my own mited observations go, it seems that, in the main they re similar to those that may provoke more lasting ymptoms I have been struck by the fact that a patient resenting with well marked sensory disturbance in a and, may for several weeks previously have noticed emporary tingling and perhaps numbness in the fingers f the same hand on awaking from sleep or sometimes fter using the hand Likewise an attack of retrobulbar euritis may be preceded by episodes of blurred vision rought on by exertion or emotion The following case s illustrative

Mrs. A aged 23 a hairdresser when playing tennis one ay in September 1953 noticed hazy vision with difficulty in eing the ball She stopped playing and after a short rest er vision became normal. Subsequently whenever she layed tennis or danced vision was temporarily blurred. In ay 1954, she began cycling to work a distance of about a ile By the time she arrived vision was so poor that she was nable to start work until she had rested for a short time oon afterwards she also noticed numbness in the right hand r some hours after cutting several customers hair in ccession.

In June 1954, vision was 6/5 both eyes, the fundi were ormal and no scotoma could be demonstrated (Mr A J B oldsmith) By July she found that even mild exertion, such s walking quickly affected her eyes to an increasing extent nd soon vision became permanently blurred By October ision was 6/60 in both eyes both discs were pale and a small ilateral central scotoma was now present

On admission in December vision had not improved and he now showed nystagmus and bilateral extensor plantar esponses. After cycling on a fixed bicycle vision became worse comparison of the scotoma in the right eye on an Amsler's hart before this exercise and after four minutes showed that t had markedly extended Five minutes later the central efect had returned to its previous size

To be distinguished, at least clinically from these ransitory initial episodes are the temporary exacerbations of symptoms which may be a sequel to an established plaque. Of 250 cases investigated by Compston and myself 82 (32%) gave a history of temporary worsening of symptoms during stress, a finding confirmed y Pratt (1951) An emotional upset may act rapidly n motor function, paræsthesiæ and vision Likewise xertion may have the same effect. These temporary hanges are of course seen in other organic conditions of he nervous system such as traumatic paraplegia but t is our impression that they occur more easily and are nduced by a larger range of exciting factors in multiple clerosis than in other organic conditions

Franklin and Brickner (1947) suggested that these hanges are due to vasospasm for they observed localized constriction of retinal arteries during episodes of blurred vision An increased vulnerability of the axis cylinder to chemical influences offers an alternative explanation

Symptom and Lesion

At first glance any attempt to correlate disturbance of function and of structure in multiple sclerosis may seem profitless However not infrequently the earliest symptoms are caused by a focal disturbance, thus permitting a clinical study of their mode of evolution I have in mind particularly sensory symptoms due to invasion of the spinal cord As Oppenheim (1911) originally pointed out tingling and numbness are usually caused by one or more plaques in the posterior columns Furthermore since the cervical cord is often attacked early in the disease a special opportunity is afforded the clinician of studying sensory symptoms since at that level afferent impulses from all four limbs and the trunk are represented in a known anatomical relationship to each other within a small area (McAlpine 1954)

Although tingling and numbness may be confined to a small area on a limb or the trunk not uncommonly they tend to spread by noting the original site of the paræsthesiæ and direction of spread it becomes evident that this is often determined by the anatomical arrangement of the proprioceptive fibres within the posterior columns. For example a spread of numbness from a hand to the shoulder and then down the homolateral trunk and finally to the lower limb is indicative of a focus in the column of Bordach extending inwards to the column of Goll. Similarly a spread may take place in the reverse direction Thus the mode of spread appears to be determined by contiguity of structure

Another feature which can be recognised clinically is the symmetry sometimes shown by plaques. For example it is not uncommon for paræsthesiæ to affect simultaneously or in quick succession corresponding parts of the lower or upper limbs, and be followed by a similar mode of spread in the four limbs A further example of symmetry is provided by retrobulbar neuritis which, contrary to many statements may affect both eyes simultaneously in multiple sclerosis This symmetrical tendency of plaques, which many years ago was commented on by pathologists poses yet another question for which at present there is no satisfactory answer

Multiple Sclerosis or Spondylosis

So far I have considered certain features of the relapsing and remitting form of the disease Presenting a striking contrast in its mode of onset and its course is the so-called progressive paraplegic or spinal form of multiple sclerosis which chiefly affects the middle-aged

In the analysis of the 309 cases already referred to I came across 27 with signs of a spastic paraplegia in which the diagnosis of multiple sclerosis was at first in doubt During the same period 31 cases of spinal cord compression due to tumour (excluding secondary deposits) came under the care of Miss Diana Beck Dr M Kremer or myself In recent years myelography has substantially reduced the number of cases of cord compression mistaken for the spinal form of multiple sclerosis Today the neurologist, while constantly aware of this pitfall, must also take into account the possibility of cervical spondylosis when confronted with a paraplegia in middle age Over the five year period already referred to there were 30 such cases. An analysis of this group and that of the 27 patients with the spinal form of multiple sclerosis showed that, while the clinical picture in the two groups was broadly similar there were certain points of difference *First the average age of onset differed* in the multiple sclerosis group it was 42 and in the cervical spondylosis group 51, the youngest patient being 27 and the oldest 68 It is in the *fifth* decade of life however that the distinction between these two causes of paraplegia may be difficult A gradual onset and slow progression of motor weakness—first in one lower limb and then in the homolateral upper limb—without any sensory symptoms or signs, may occasionally occur in the progressive form of multiple sclerosis, none of our cases of myelopathy associated with cervical spondylosis showed this pseudohemiplegic type of progression In multiple sclerosis short attacks of tingling and numbness, usually brought on by exertion, may antedate motor weakness by weeks or months, but such a history is rarely obtained in cervical spondylosis The spread of paræsthesiæ, when it occurs in multiple sclerosis, tends to be much more rapid than in spondylosis Pain in the upper or lower limbs is a well recognised feature of the early phase of spondylosis, yet it was not a rare symptom in this small group of multiple sclerosis patients, being among the presenting symptoms in 8 of the 27 cases, it was usually referred to one or both lower limbs or the back Scattered references to pain in this disease can be found in the literature, and since its interpretation remains in doubt it is worthy of further study

A history of early disturbance of sphincter control was found more commonly in multiple sclerosis as compared with the myelopathy of spondylosis, the figures being 14 of the 27 multiple sclerosis cases compared with 8 of the 30 spondylosis patients An episode of temporary incontinence early in the history should suggest multiple sclerosis

The course of the spinal form of multiple sclerosis is sometimes interrupted by a superimposed relapse, this occurred in 3 cases in this series in the form of paræsthesiæ which developed over the course of a few days and then receded I have not met with similar episodes in the myelopathy of spondylosis

Regarding signs, the upper limb reflexes afford little help in differentiating between these two groups of patients—particularly depression or absence of one or more of these reflexes, since this occurred with almost equal frequency in the two groups While muscular wasting in the upper limb was relatively more common in the spondylosis group, 2 cases of tetraplegia due to multiple sclerosis showed wasting of the intrinsic muscles of the hands, a finding which was commented upon by Déjerine (1884) when he drew attention to the similarity between this form of the disease and amyotrophic lateral sclerosis

The presence of nystagmus proved to be the most helpful single diagnostic sign it was present in 14 of the multiple sclerosis cases, but in only 4 of those with spondylosis In these 4 patients it was purely horizontal in type and was associated with evidence of involvement of the upper cervical cord as judged by exaggeration of some of the upper limb reflexes or by radiological evidence of spondylosis as high as C3–4 In the multiple sclerosis group a well marked rotatory or monocular nystagmus was not unusual and provided evidence of an extraspinal lesion

Apart from nystagmus, evidence of one or more lesions above the level of the spinal cord was found in 9 of the multiple sclerosis cases, unilateral temporal pallor of the discs (4 cases), mild dysarthria (3 cases), and an exaggerated jaw-jerk (2 cases) Euphoria was noted in 2 patients but only in the course of a follow-up when symptoms had been present for several years

The findings in the cerebrospinal fluid proved of the utmost value, particularly in those cases in which signs were confined to the spinal cord 12 of the 27 multiple-sclerosis patients showed a marked paretic curve, in 6 others there was a mid-zone curve of at least 2's In 1 case the only abnormality was a rise in the protein figure, in the remaining 8 cases the fluid was normal on one or more occasions By contrast, a mid-zone curve of 2's was only found in 2 cases of cervical spondylosis, in the remaining 28 cases the Lange curve was normal

Before leaving these two groups of patients, I wish briefly to refer to 8 cases in the multiple sclerosis group which showed clear evidence of cervical spondylosis The youngest patient was 31 at the onset of symptoms and the oldest 51, with an average age of 42 The diagnosis of multiple sclerosis in these patients with cervical spondylosis was based on the points already mentioned, with the addition of myelography in two cases In 2 cases protein figures of 130 and 120 mg. per 100 ml were found

A woman, aged 44, had for two years received treatment for pain in the neck and left arm due to well marked cervical spondylosis Rather abruptly she began to stagger when walking and she was admitted under the care of my colleague Dr Kremer Among the positive signs were a pronounced monocular nystagmus, limb ataxia, a mild paraparesis, and a strongly paretic gold curve She responded only slightly to traction and some months later was readmitted with an abrupt progression of symptoms

The second case was a male, with onset of symptoms at the age of 31, who five years later was dysarthric and showed temporal pallor of one disc and nystagmus. There was no evidence of block on flexion and extension of the head during lumbar puncture

It is probable that in these two patients the spondylosis accounted in some degree for the high protein figure. A marked rise in protein occurs rarely in uncomplicated cases of multiple sclerosis For example, only 5 out of 512 spinal fluids from cases of multiple sclerosis examined by the Courtauld Institute at the Middlesex Hospital showed a figure of 100 mg, or more, per 100 ml

Conclusions

Certain of the facts mentioned in this lecture may be summarised as follows

First, of the chronic organic nervous diseases occurring in the British Isles, multiple sclerosis now appears to be the commonest The surveys of Northern Ireland and Northern Scotland show that in these parts of our islands at least one adult in every 1[illegible] is affected by it The figure for England and Wales is probably only a little behind this one.

Secondly, there is a small but significant familial incidence varying in Great Britain from 5% to just over 10% Since it is exceptional to find more than two members of a family, whatever its size, affected by the disease, it must be assumed that when present the genetic influence is usually weak and must be reinforced by constitutional or environmental factors before the nervous system is attacked, and furthermore, that the disease may develop in the absence of any obvious genetic influence

Thirdly, in some patients a variety of factors, including ill health, an infection, trauma, and emotional stress may precipitate not only the onset of the disease, but also relapses

The fourth fact about the disease concerns its abrupt onset and the natural tendency for symptoms to remit and later recur—features which for many years have been recognised as likely to provide a clue as to its ætiology

Lastly, the considerable variation in the behaviour of the disease in its earlier stages must depend on the individual's reaction to it

The Allergic Theory

For too long our attention has been fixed on the nervous system in multiple sclerosis Detailed though the average history may be regarding events relating to this system, account is seldom taken of the recent and past general medical history Yet it is in the medical background of these patients that we must look for the events which in a small proportion of the population initiate changes in the myelin sheath Of recent views as to the cause of the disease, the so called allergic theory is perhaps the one most acceptable to the clinician The occasional familial incidence, the nature and variety of the precipitating factors, the presence of some other form of allergy, before or after the onset, in a significant proportion of cases, an abnormal sensitivity to drug d lastly the abrupt onset and characteristic relapsing d remitting course—all these factors may be cited in pport of the view that multiple sclerosis represents a pe of immunity reaction in the central nervous system cAlpine and Compston 1952)

Since confirmation or otherwise of this hypothesis ay be long delayed perhaps it is permissible to consider e nature of the hypothetical sensitising agent or agents. general allergens are derived from bacteria from otein derivatives and from drugs Since the breakdown oducts of bacteria constitute their commonest source, appears likely that, if sensitisation plays any part in e genesis of multiple sclerosis, an infection initiates e process, at least in some patients However, in ractice it would be difficult to prove such a relationship -first because of the time lag that might theoretically ccur between the infection and the first clinical evidence f the disease (McAlpine 1946) and secondly because s Rich (1947) has pointed out in discussing the question f allergy once a tissue has become sensitised it may bsequently react to a wide range of substances Sup ort for the idea of a latent or asymptomatic phase of ultiple sclerosis comes from a consideration of the part layed by the so called precipitating factors. These are learly not strictly causal but in the words of Lumsden, 'either they fire off or trigger' an intrinsic self propa ating mechanism, or they provoke the onset of symptoms n connection with areas of the white matter already nvolved by the disease process' (McAlpine Compston nd Lumsden 1955) The second of these postulates eems probable and is consistent with the theory of llergy

ourse of the Disease

This leads me to consider briefly certain features of arly symptomatology and the light they may throw on he nature of the initial change in myelin sheath Tran itory and recurrent symptoms such as diplopia, blurred ision and paræsthesiæ, which in some patients may onstitute the earliest evidence of the disease, could be xplained on the basis of the so-called shadow plaque eferred to by Lumsden (1951) In this stage of partial emyelination it is not difficult to imagine that the nderlying axis cylinder might react abnormally to a ariety of stimuli If the concept of an initial asympto matic phase of the disease be accepted, does demyelination egin during this period or is there a stage of pre emyelination in which the complex cytochemical alance of the sheath is in some way altered?

In 1903 Williamson, of Manchester was struck by the imilarity between the pattern produced by the applica ion of a soluble dye to the cut surface of the spinal cord nd the mode of development of plaques In 1933 Hallervorden and Spatz drew attention to the occasional ccurrence of a ring formation in the early plaques of multiple sclerosis similar to that observed in Balo s oncentric sclerosis. They attributed this type of forma ion to diffusion outwards from a central focus as in the o-called *Laesegang* phenomenon a subject recently iscussed by Lumsden (McAlpine Compston and Lumsden 1955) The tendency for early symptoms articularly paræsthesiæ to spread according to contigu ity of structure lends support to the possible rôle of a rocess of diffusion

The next question concerns the important issue as o whether arrest of the disease is ever possible For the athologist this seems unlikely since plaques tend to volve slowly and progressively On the other hand the linician is aware of cases in which after one or more pisodes no fresh evidence of the disease is apparent for many years and even in some instances for the rest of the patient s life Unless there is a system for following up arly cases most of these patients will be missed for they may have no occasion to report either to their general ractitioner or to hospital From my own observations I am satisfied that the incidence of these mild cases with a good resistance to the disease is rather higher than is generally supposed

It may be possible to reconcile these differing view points of clinician and pathologist The manner in which early symptoms clear up and may remain in abeyance for several years emphasises the potential reversibility or at least non progression of the early lesion; by contrast we are well aware of the probable course when paraplegic or cerebellar signs become established It is in this type of case that we can understand the evolution of the plaque as seen in the post mortem room

Treatment

Lastly brief reference must be made to the present unsatisfactory attitude towards treatment This attitude is determined by two beliefs—first that a serious degree of disability is inevitable in all cases however treated and secondly that treatment consists solely in palliative measures I have already pointed out that the prognosis as a whole is less unfavourable than was formerly thought and in some patients the disease runs a relatively benign course As regards treatment, the lack of an effective remedy should not blind us to the necessity of adopting a more positive attitude towards these patients, particu larly in the early stage of the disease before irreversible changes in the nervous system have taken place Assum ing that constitutional factors are important in the ætiology of multiple sclerosis, then it is our duty first to ensure an adequate period of rest in bed after the onset or a relapse followed by a long period of convales cence and secondly, to increase as far as possible the patient s resistance to the disease by close attention to physical and mental health over the first few crucial years

Owing to its capricious behaviour the assessment of treatment in multiple sclerosis has always presented difficulties. Yet the necessity of devising a method of evaluating a particular remedy is obvious Compston (1953) has suggested a formula by which the relapse rate before and after treatment can be compared. This method however does not cover the effect on recent symptoms

After consultation with Dr Richard Doll a form of trial has been devised in which a control group of patients can be used Briefly the trial is divided into two parts. The first enables a comparison to be made of the effects of treatment during a month s stay in hospital in two groups of patients one on the drug under trial and the other on some form of recognised treatment such as arsenic The object of the second trial is to assess the effect of the drug on the relapse rate It is hoped that experience gained during the next year will show the value of these two forms of trial

I would like to conclude with two observations The natural history of multiple sclerosis suggests that it is not due to a single cause but to the interplay of a number of factors—genetic constitutional and environmental Despite its complexity we as neurologists should not be content to leave this problem to the laboratory worker but with widened outlook should endeavour to play a part in its solution

REFERENCES

Allison, R S (1950) *Brain*, 73 103
— Millar J H D (1954) *Ulster med J* 23 suppl 2
Bing R. Reese, H (19 6) *Schweiz med Wschr* 56 30
Bramwell B, (1917) *Edinb med J* 18 16
Compston, N D (1953) *Lancet* ii 471
Curtius, F (1933) Multiple Sklerose und Erbanlage Leipzig
— Speer H (1937) *Z ges Neurol. Psychiat* 160 226
Déjerine J (1884) *Rev med Paris* 4 193.
Franklin C. R. Brickner R. M (194) *Arch. Neurol Psychiat Chicago* 58 125
Gram H C (1934) *Ugeskr Læg* 96 823
Hallervorden, J Spatz H (1933) *Arch Psychiat Nervenkr* 98 641.
Hoesslin von R (1934) Über Multiple Sklerose München.
Keschner M. (19 0) *Proc Ass Res nerv Dis* 28 533.
Kurland L. T (1952) *Amer J Hyg* 55, 457
Lumsden C E (1951) *Brit med J* i 1035

References continued overleaf

A VALUATION OF HYDROCORTISONE OINTMENT

BRIAN RUSSELL
M.D Lond, F R C P, D P H
PHYSICIAN-IN CHARGE

J S PEGUM
M A Camb, M.D Lond, M R C P
ASSISTANT PHYSICIAN

N A. THORNE
M D Lond, M R C P
SENIOR REGISTRAR

R V GRANGE
M B Camb
REGISTRAR

SKIN DEPARTMENT, LONDON HOSPITAL

REPORTS from the United States and elsewhere indicate that hydrocortisone (17-hydroxycorticosterone, or compound F) ointment is highly effective in the treatment of various pruritic dermatoses

Sulzberger (1954) found it helpful in infantile eczema, atopic (pruriginous) dermatitis, contact eczematous dermatitis, otitis externa, nummular eczema, seborrhœic eczema, pruritus ani et vulvæ, exfoliative erythroderma of eczematoid or seborrhœic type, and some cases of eczematous and lichenified eruptions of the hands, feet, eyelids, face, neck, and genitalia, also in the "distinctive exudative, discoid, and lichenified dermatosis" of Sulzberger and Garbe Hydrocortisone has proved ineffective in pemphigus vulgaris, lichen planus, alopecia areata, psoriasis, and discoid lupus erythematosus, it does not inhibit the development of erythema from exposure to ultraviolet rays (Everall and Fisher 1952)

Alexander and Manheim (1953) and Malkinson and Wells (1954) have formed similar opinions, but they consider that hydrocortisone is ineffective in general exfoliative dermatitis, autosensitisation, and "-ide" (bacterial or fungous allergy) eruptions

McCorriston (1954), using hydrocortisone ointment in various vehicles, obtained 75–100% relief in 104 children and infants with eczema

Robinson (1953) obtained dramatic relief in 20 of 28 patients with atopic dermatitis, in 5 of 8 patients with pruritus vulvæ, and in 1 of 3 patients with pruritus ani 1 patient with discoid lupus erythematosus showed a good response and 2 showed fair responses

Sidi et al. (1953) state that the most striking effect is on pruritus, the action being immediate and lasting for at least twelve hours They used it for exogenous, allergic, seborrhœic, nummular, and purpuric eczemas, for pruritus, for chronic dermatitis of the eyelids, and for various other dermatoses

Goldman and Preston (1954) treated 22 cases of poison ivy dermatitis, with excellent results in 3, slight changes in 5, and no change in 14 cases

These reports suggest that hydrocortisone ointment relieves itching and reduces the manifestations of inflammation in a number of skin diseases, but in none of the above trials were concealed controls employed In the trial of any new treatment for pruritic conditions it is important to eliminate as far as possible the influence of suggestion, particularly when physical signs are slight and reliance has to be placed on subjective impressions

When anti histamine drugs were introduced, it was soon reported that they were effective local applications for the relief of itching Many of these claims were based on uncontrolled trials, on comparisons with previous remedies, or on trials which employed contralateral controls Later, Baldridge (1951) treated 41 patients with 5% phenindamine ('Thephorin') ointment on one side and its unmedicated base as a control on the other These were presented as "slightly different forms of the same medication" to the patients who were asked to estimate the percentage of relief on the two sides 47% of the areas treated with thephorin were reported as relieved, and 49% of the areas treated with the unmedicated base were reported as relieved Many dermatologists now agree that most anti histamine drugs are useless when applied topically

It can be said of contralateral controlled trials that at least four fallacies may invalidate the results

(1) Absorption may lead to remote as well as local effects

(2) The trial substance may inadvertently be transferred to the opposite side

(3) Unless the lesions on the two sides are of equal intensity and duration, they are not strictly comparable (e g, the response to treatment of an eczematide cannot be compared with that of the primary lesion—perhaps an area of unilateral hypostatic eczema—from which it developed) This difficulty can be overcome by random allocation of treatment and control to right and left sides, but even then, unless a large number of patients are included in the trial, the results may prove inconclusive

(4) There may be a *Mitreaktion* (Siemens 1951, 1953) in which, when a patch of skin disease is treated on one side of the body, untreated areas on the opposite side also show improvement This may be the result of a spinal reflex, or it may be accounted for by the reduction in the amount of circulating histamine which follows treatment.

The Present Trial

In assessing the value of hydrocortisone ointment ('Hydro Cortisyl,' Roussel), we used concealed, alternating, self contained controls, the patients themselves recorded their daily progress over fourteen consecutive days on cards supplied to them each week

CONTROL BY ALTERNATION

A trial in which (*a*) the vehicle alone and (*b*) the substance being tested are used alternately in treatment has much to commend it, provided certain criteria are observed, and certain uncontrollable factors are appreciated

1 The number of patients tested in each group must be sufficiently large

2 The patient should be unaware that an ointment containing a trial substance is being tested against the ointment alone

3 The clinician should not know when the patient receives the trial ointment and when he receives the vehicle alone until the specified period of the trial has been completed and all data have been recorded

4 It is possible that either substance will continue to exert some effect during the first few days after replacement by the other Thus the test remedy (or the vehicle alone) when applied during the second week may appear more (or less) effective than in the first week

5 The days of starting treatment should be evenly distributed through the week so as to spread the possible influence of weekends and bank holidays

6 The influence of menstruation is unlikely to be important if patients are introduced to the trial as they attend for treatment, without reference to the stage in the monthly cycle

7 If the whole trial covers several months, and preferably a year or more, and if patients enter it at various times, the influence of seasonal climatic changes is unlikely to be important

8 The influence of extraneous factors such as fatigue, emotional disturbances, &c, may affect individual results Such factors should be noted at each attendance

9 Any record keeping by the patient is an abnormal state of affairs In suggestible patients results may prove better than might be expected, in very conscientious patients over-attention to the skin may cause increased awareness of itching Both possibilities are likely, not only with the

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DR MCALPINE REFERENCES—*continued*

McAlpine, D (1946) *Brain*, 69, 233
— (1954) Fifth International Neurological Congress, Lisbon Comptes rendus 4, 198 *Arch Middx Hosp* n s 4 1
— Compston N D (1952) *Quart J Med* 21, 135
— — Lumsden C E (1955) Multiple Sclerosis Edinburgh
Müller, R. (1949) Studies on Disseminated Sclerosis *Acta med scand* suppl 222
Oppenheim H (1911) *Brit med J* ii 729
Pratt R. T C (1951) *J Neurol Psychiat* 14 326
— Compston N D McAlpine D (1951) *Brain*, 74, 191
Rich A R. (1947) Hypersensitivity in Disease *Harvey Lect* 1946–47
Sällström T (1942) *Acta med scand* suppl 137
Willia T (1902–03) *Manchr med Rev* 4 4th ser 261

vehicle but with the test substance as well. Reciprocal short-term trials are a useful means of determining the worth of a new remedy for chronic benign cutaneous reactions: the patient runs no risk and suffers no inconvenience if the vehicle is harmless; the vehicle may in fact prove helpful in itself.

THE RECORD CARDS

'Record of itching' cards, adapted from cards used by Hodgkinson (1954) for controlled clinical trials of analgesic drugs, were designed for the trial as follows:

RECORD OF ITCHING

Date

Patient's Name Record No

	Very good day (no itching)	Fair day (less itching)	Average day (usual itching)	Bad day (more itching)
Sun.				
Mon.				
Tue.				
Wed.				
Thu.				
Fri.				
Sat.				

Place X in appropriate space each morning for previous day

The patient's name and record number and the date were entered by the clinician, and a mark was made to show on which day of the week the trial began. The patient's attention was then drawn to the request at the foot of the card: "Place X in appropriate space each morning for previous day." The appropriate spaces recorded whether the patient had had a "very good day" (no itching), a "fair day" (less itching), an "average day" (usual itching), or a "bad day" (more itching).

The patients were unaware that two different preparations were being given to them. They were informed that it was desired to find the worth of a remedy and that for this purpose a trial lasting two weeks was necessary. No "salesmanship" was employed, and the use of superlatives or of such adjectives as "American" and "special" was avoided. On the contrary, a restrained remark such as the following was made: "Please apply the ointment very thinly twice a day and record its effects on this card." At the second attendance, no matter what the result of the first week's treatment had been, a comment was made such as the following: "A fortnight's treatment is needed to give the remedy a thorough trial. It is best to have a fresh supply. Please discard any ointment that remains and indicate results on this card for another week." All patients coöperated well and seemed to understand what was required of them. There were no 'spoiled papers'.

The method of prescribing was to write on the standard outpatient prescription card: "HC ung trial 1st (or 2nd) week 5 g, store no. 1." The patients were told that only a small quantity of ointment could be provided for one week's treatment, and they were sent to a special section of the outpatient dispensary. This enabled concealed records to be made and kept by one pharmacist, who was also responsible for arranging an approximately equal distribution between the A B (hydrocortisone→vehicle) and the B A (vehicle→hydrocortisone) trials. He did this by alternating the A B and the B A sequence. This resulted in a random distribution because there were eight different skin conditions included in the trial. There were 66 patients in the A B sequence and 63 in the B A, while 3 patients did not complete the trial. We four clinicians had no means of telling which patients received the A B and which the B A sequence, because we did not know when one of us had introduced a new patient to the trial—or for that matter the order in which the patients arrived at the dispensary. 5 g of ointment or base was dispensed as a rule, but sometimes 10 g was given. The control ointment (of propylene glycol, polyethylene glycols, and zinc stearate) was the same as the vehicle for the 2.5% hydrocortisone acetate ointment; the two ointments were identical in appearance. Identical plastic ointment boxes were used for the trial substance and for the base. They were not labelled in any way to indicate the nature of the contents. At the end of each fortnight's trial the pharmacist was asked to divulge the treatment that had been given each week, so that a decision might be made on the future treatment of that patient. Progress notes were also made at each attendance, the patient's verbal descriptions being recorded; these made a valuable parallel study to the record cards. Changes in physical signs were also recorded.

In some of the conditions—e.g., anogenital pruritus—physical signs were often slight or absent, the changes being mainly or entirely subjective. In patients with multiple lesions—e.g., some cases of discoid eczema—the trial ointments had to be applied to one area only, while the remaining lesions were treated with some other bland local application. As far as possible sedatives were withheld during the trial period; if they were necessary, they were given for both weeks in identical doses.

On inspecting both cards, and after allowing for carry-over effects, it was usually easy to decide which preparation was the more effective. The subjective results recorded during the last day or two of a week's trial were often poorer than during the middle of the week. We believe that this was often due to the necessity for very sparing use of the ointment towards the end of each week because of the small amount (5 g.) that was usually supplied.

In cases where the 2.5% hydrocortisone ointment proved more effective than the base alone, treatment was continued with 1% hydrocortisone ointment. Sometimes treatment was continued with the base and a change-over to 2.5% or 1% *hydrocortisone ointment* was made after a further week or two without the patient's knowledge. It was thus possible to clarify inconclusive impressions gained from the first trial. It was also possible to compare the efficacy of 2.5% with 1% hydrocortisone ointment; sometimes the 2.5% preparation was necessary for complete control, in others 1% was sufficient.

MATERIAL

Included in the trial were 132 patients (72 males and 60 females), with the following conditions:

25 with anogenital pruritus.
21 with lichen simplex.
12 with infantile eczema.
22 with Besnier's prurigo.
23 with discoid eczema.
11 with chronic idiopathic eczematous dermatitis of the hands.
11 with otitis externa.
7 with pruritic psoriasis, *mostly anogenital*.

RESULTS

Points were allotted daily to each patient studied, allowing 2 points for complete relief, 1 for partial relief, 0 for no change, and −1 for *worsening*. *These numerals* indicate trends only and in no way imply degrees or percentages of relief. The points scored are recorded on block diagrams in figs. 1–8. These show great individual variations of subjective relief. We have thought it valid to summarise the effects obtained in "hydrocortisone" and "vehicle" groups during the week of their application. The daily means are set out in table I.

The number of patients in a few of the groups was too small for dogmatic statements, but it is clear from this table that appreciably greater *improvement* sometimes resulted from the use of hydrocortisone. No absolute criterion of efficacy can be applied, but on the above rating the results may be summarised thus:

Lichen simplex, discoid eczema, and otitis externa.—The results were strongly in favour of hydrocortisone.

Infantile eczema and idiopathic eczematous dermatitis of the hands.—The results, though apparently in favour of hydrocortisone, were less conclusive.

Pruritic anogenital psoriasis.—The results were equivocal. In the course of treatment with hydrocortisone ointment 6 patients improved and 1 worsened, while with the vehicle alone 5 patients improved and 2 worsened. This suggests that the vehicle was responsible for the improvement.

Besnier's prurigo.—Slightly better results were obtained with the vehicle alone, but neither hydrocortisone nor the vehicle produced very good results. Undoubtedly the trial was often inadequate in this condition, because the cost and scarcity of hydrocortisone made it advisable to use it only on the worst, lichenified areas in these patients. Nevertheless, clinical and electro-encephalographic evidence (Ingram 1955, Russell and Last 1955) indicates that this disease affects the whole ectoderm (nervous system and skin), so it is not surprising that local treatment by itself should prove ineffective.

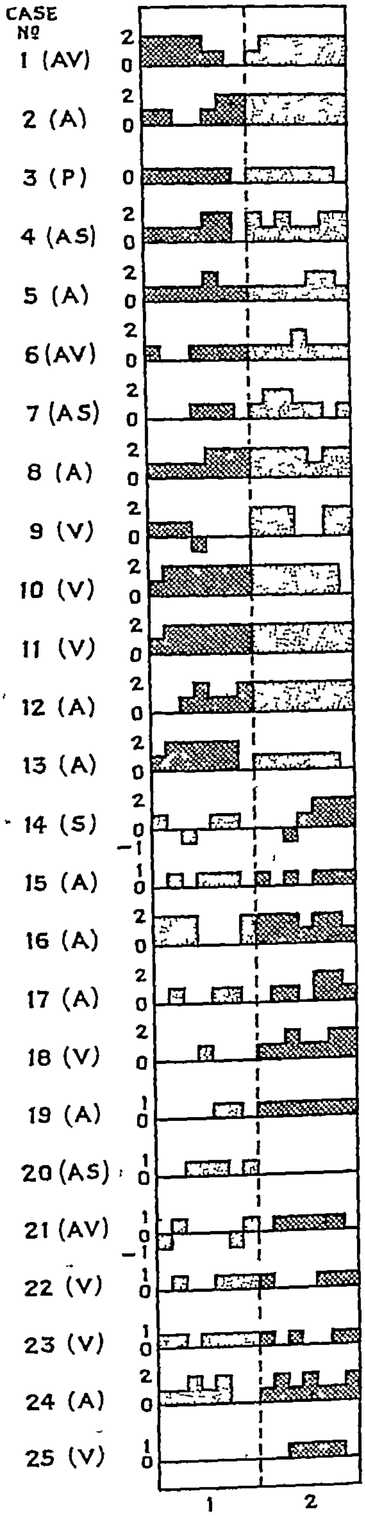

Fig 1—Results in 25 cases of anogenital pruritus.

A = anal P = perineal

S = scrotal V = vulvar

Anogenital pruritus.—Slightly better results were obtained with the vehicle alone. Nevertheless excellent longer-term results were obtained in this condition with hydrocortisone (see below), 32% of patients being completely relieved and another 24% much improved. We can only suggest that our equivocal findings in the "switch-over" trial were due to one or more of the following factors: the shortness of the trial, the undoubted efficacy of the vehicle itself, the carry-over effects from one week to the next, and, in some cases, the influence of suggestion. There was no obvious difference between the results obtained in anal pruritus and in genital pruritus. Patients with distinct physical signs—chiefly lichenification—responded best, and those without physical signs responded worst. This is not surprising, for pruritus without physical signs is probably of central origin.

SIDE-EFFECTS FROM HYDROCORTISONE OINTMENT

Remote Effects

We have seen no evidence of remote ill effects following the use of hydrocortisone ointment.

Smith (1953) found no significant change in the eosinophil count after the inunction of 6 g. of 2.5% hydrocortisone-acetate ointment, and he thought it unlikely that amounts of hydrocortisone so small as to escape detection could account for the therapeutic effects reported. No systemic ill effect has been reported from the prolonged application of hydrocortisone ointment.

Local Irritation, Sensitisation, and Aggravation of Infective Dermatoses

In the series of Malkinson and Wells (1954) irritation developed in 4 of 71 patients treated, and the treatment was stopped, but no case of sensitisation to hydrocortisone has yet been reported. There were no cases in our series. 3 of Robinson's (1953) patients complained of increased burning and itching when the ointment was applied, and 2 of them were found to be sensitive to the lanolin in the ointment base. The ointment used in the present trial did not contain lanolin. A few of our patients stated that it was "too drying," but the great majority found it comforting and aesthetically acceptable. The occasional complaint of undue dryness can be overcome by having an alternative vehicle of hydrous ointment type, but the routine use of a greasy vehicle of this sort would be liable to cause maceration of the skin at some sites.

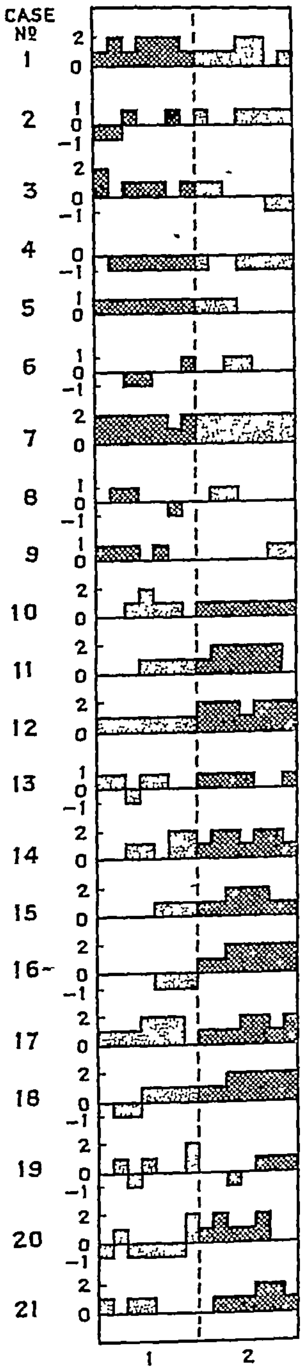

Fig 2—Results in 21 cases of lichen simplex.

3 of our patients abandoned the treatment and were not included in the tabulated results. They were:

1. A patient with discoid eczema who complained that the ointment "burned." She was receiving the vehicle alone at the time. She refused to attend again for patch testing, on the grounds that the dermatosis had cleared up with treatment for her "nerves."

2. A patient with chronic eczematous dermatitis of the hands, of unknown cause, who complained of fresh outcrops of vesicles after applying hydrocortisone ointment for three days. She abandoned its use. Patch tests with the hydrocortisone ointment and with the vehicle alone were negative, but when patch testing was carried out with the separate constitutents of the vehicle, a positive response was obtained to propylene glycol. Her dermatitis subsequently improved

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KEY TO FIGS 1–8.

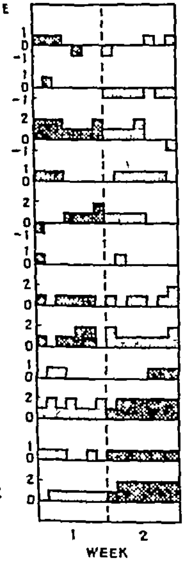
Hatched = hydrocortisone. Stippled = vehicle. 2 = no itching. 1 = diminished itching. 0 = usual itching. −1 = increasing itching.

ly when 2·5% hydrocortisone, with hydrous ointment as ehicle was applied. This had been specially prepared r request.

A patient with otitis externa, whose ears became more en and exudative shortly after he began treatment with ocortisone ointment. His eyes also became swollen. Cul revealed *Staphylococcus pyogenes*, *streptococcus hæmolyticus* *Pseudomonas pyocyanea*. Patch tests with hydrocortisone with the vehicle were negative.

alkinson and Wells (1954) did not find that secon ly infected dermatitis was aggravated by the drug.

The anti-inflammatory action of hydrocortisone relieves itching and lessens scratching, thus diminishing bacterial contamination of the lesions and bringing about amelioration of the infective as well as of the eczematous and lichenified elements. On the other hand, dermal infections with cocci (such as erysipelas, boils, and ecthyma) should in theory be aggravated by hydrocortisone, which has the effect of lowering the resistance of the host, thus enabling the organisms to multiply (Houghton 1954, Hart 1954). This matter is still sub judice.



3—Results in 12 cases of infantile eczema.

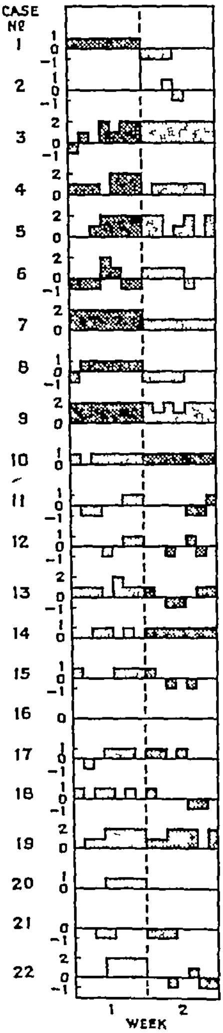


Fig 4—Results in 22 cases of Besnier's prurigo.

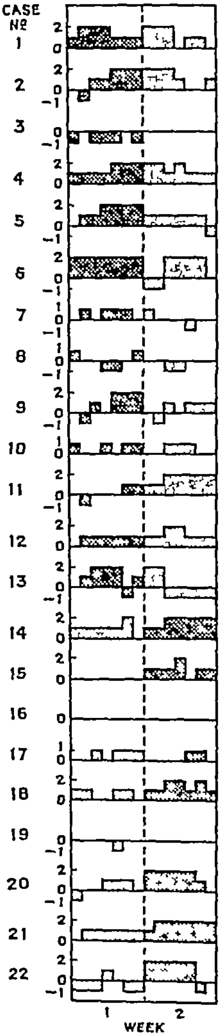


Fig 5—Results in 23 cases of discoid eczema. The 23rd patient failed to complete the trial.

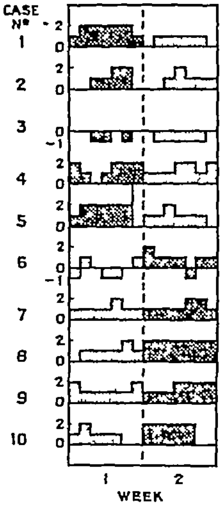
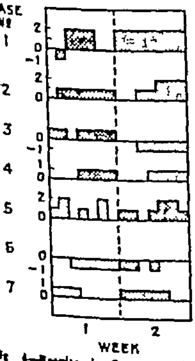


Fig 7—Results in 11 cases of otitis externa. The 11th patient failed to complete the trial.



6—Results in 7 cases of pruritus of anogenital region.

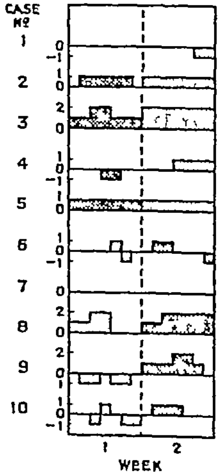


Fig 8—Results in 11 cases of eczematous dermatitis of hands. The 11th patient failed to complete the trial.

TABLE I—MEAN DAILY RESPONSE SCORES

Diagnosis	No of cases	Score with hydrocortisone	Score with vehicle
Anogenital pruritus	25	1 01	1 04
Lichen simplex	21	1 00	0 49
Infantile eczema	12	0 84	0 55
Besnier's prurigo	22	0 54	0 59
Discoid eczema	23	0 97	0 57
Idiopathic eczematous dermatitis of the hands	11	0 61	0 43
Otitis externa	11	1 28	0 79
Pruritic anogenital psoriasis	7	0 63	0 51

EFFICACY OF THE VEHICLE

In trials such as this it is always possible that the bland vehicle may have a considerable antipruritic action

Sulzberger and Witten (1952), in their early trials of hydrocortisone, noted some improvement with the ointment base alone, though less than with the ointment containing hydrocortisone McCorriston (1954), too, noted that in a number of patients the control sites of the soft paraffin and emulgent bases showed some improvement This was confirmed in a later study by Sulzberger et al (1953) Most of their patients were treated with hydrocortisone acetate in a non greasy base (containing zinc stearate, propylene glycol, polyethylene glycols, and water)

Robinson (1953) noted that after the condition had been controlled by hydrocortisone, it often seemed to respond better to other local therapy than previously

McCorriston has used hydrocortisone in four different vehicles in the treatment of infantile eczema These were a cream of zinc stearate, propylene glycol, polyethylene glycols, and water, white soft paraffin, a jelly base, and an oil in-water emulgent base Though the cream was useful in the weeping stage, the jelly was found to be too drying The soft paraffin or the emulgent base were preferable for dry, thick, scaly areas

In the present trial the vehicle was similar to that used by Sulzberger and Witten (1952)—namely, a non greasy polyethylene glycol base Polyethylene glycols (Smyth et al 1950) have proved less irritant than soft paraffin mild sensitisation reactions (faint erythema) as almost as common as with lanolin, soft paraffin, simple cerate, and simple ointment Case reports of sensitivity to polyethylene glycols are very few Strauss (1950) reported 2 cases of sensitivity to the entire group of polyethylene glycols These substances are non-ionic (Schutz 1953), they are therefore insensitive to metallic ions, and can be used both in acid and in alkaline media They dissolve or emulsify lipophilic substances and are valuable vehicles for oil soluble drugs when it is desired to bring these into close contact with the skin and with its folds

Results obtained with the vehicle in the present study indicate that it is remarkably effective by itself as an emollient and as an antipruritic agent, but its efficacy is far less than that of hydrocortisone ointment in of the skin diseases that we have studied

From the cosmetic point of view, a non greasy b of the "vanishing" type is more pleasant than a greasy ointment We agree with Sidi and Bourgeois Gavardin (1953) that the polyethylene-glycol base has an action superior to that of most local applications, and it has the advantages of being æsthetically acceptable and not necessitating dressings

TABLE II—INDEPENDENT ASSESSMENT OF EFFECT OF HYDROCORTISONE OINTMENT

Disorder	Cleared without relapse	Completely controlled	Much improved	Slightly improved	Unchanged	Worse or course abandoned
Anogenital pruritus	2	6	6	8	2	1
Lichen simplex	0	2	8	3	7	1
Infantile eczema	0	2	0	6	4	0
Besnier's prurigo	0	2	1	7	11	1
Discoid eczema	2	3	4	4	9	1
Idiopathic eczematous dermatitis of the hands	0	1	2	1	5	2
Otitis externa	2	3	2	2	1	1
Pruritic anogenital psoriasis	1	0	1	1	4	0
Total	7	19	24	32	43	7

SUBSEQUENT PROGRESS

With more prolonged treatment (without concealed control or record cards) progress has been maintained in lichen simplex, discoid eczema, anogenital pruritus, and otitis externa As extraneous events have a powerful influence on progress in infantile eczema, hydrocortisone ointment, though often helpful, may have to be assisted by sedative drugs In cases of Besnier's prurigo we have not felt justified in continuing treatment with hydrocortisone

INDEPENDENT ASSESSMENT

An independent observer (Dr C M Ridley) has perused the case notes and analysed the results. The assessment (table II) was made on subjective impressions combined with the objective evidence recorded in the notes, it attempted to measure the effect from the beginning to the end of treatment with hydrocortisone ointment The duration of treatment varied from two weeks to several weeks In some cases treatment with hydrocortisone ointment was still in progress at the time of the assessment

CONTACT ECZEMATOUS DERMATITIS

We have observed marked relief of contact eczematous dermatitis with hydrocortisone ointment However, the condition does not lend itself to controlled studies, its natural course differing greatly from one person to another

Summary

Concealed trials with hydrocortisone ointment, alternated with its vehicle alone, and a longer term independent survey of results, have shown that hydrocortisone was remarkably effective in many patients with lichen simplex, discoid eczema, otitis externa, and anogenital pruritus In infantile eczema and in idiopathic eczematous dermatitis of the hands the improvement was less obvious In Besnier's prurigo local improvement was sometimes obtained, but the general results were poor one reason for this may have been that the ointment applied in very small quantities In itchy psoriasis of the anogenital region the results apparently depended on the efficacy of the vehicle

Hydrocortisone ointment is also highly effective in contact eczematous dermatitis, but examples of condition have not been included in these controlled

An independent observer, assessing the results, cluded that there had been distinct or complete relief in 14 of 25 patients with anogenital pruritus, in 10 of with lichen simplex, in 2 of 12 with infantile eczema, in 3 of 22 with Besnier's prurigo, in 9 of 23 with discoid eczema, in 3 of 11 with idiopathic eczematous dermatitis of the hands, in 7 of 11 with otitis externa, and of 7 with itchy flexural and genital psoriasis

Only 1 of the 132 patients in the trial proved sensitive to the vehicle, but relief was subsequently obtained with hydrocortisone in hydrous ointment 1 patient complained that the ointment caused a burning sensation in another infection increased during treatment

We wish to thank Dr L Bernstein, of the department of physiology of the London Hospital, for his statistical guidance and constructive criticism, and Dr A E Gremeaux, of Roussel Laboratories, for his coöperation, and for supplying the hydrocortisone ointment and the inert vehicle which we sed in the trial We also thank Mr D C Phillips of the harmaceutical department of the London Hospital, who ersonally supervised the concealed trial

REFERENCES

lexander R. M., Manheim, S D (1953) J invest. Derm. 21 223
aldridge G D (1951) Arch Derm Syph Chicago 63 260
verall, J., Fisher L (1952) J invest Derm. 19 97
oldman, L Preston R. H (1954) J Amer med Ass 154 1318
art P D A (1954) Brit med J ii, 768
odgkinson, R. (1954) Therapeutic Notes (Parke Davis) no 3 p 7
oughton L E (1951) Lancet, i 595
ngram, J T (1955) Brit J Derm 67 43
cCorriston, L. R. (1954) Canad med Ass J 70 59
alkinson, F D., Wells, G C. (1954) Brit J Derm 66 300
obinson, R. C. V (1953) Bull Johns Hopk. Hosp 93 147
ussell, B., Last, S L (1955) Brit. J Derm. 67 65
chulz, E. (1953) Arzneimittel-Forsch 3 451
idl, E., Bourgeois-Gavardin J (1953) Pr méd 61 1700
— — Plas, G (1953) Ibid p 997
enens, H W (1951) Hautarzt 2 430
— (1952) Ibid 3 463
mith C. D (1953) Arch Derm. Syph Chicago 68 50
myth H F jun., Carpenter C P Weil C S (1950) J Amer pharm. Ass. 39 349
rause, M. J (1950) Arch. Derm. Syph. Chicago, 61 420
ulzberger, M B., (1954) In Modern Trends in Dermatology Edited by R. M. B, MacKenna. London
— Witten, V H (1952) J invest Derm 19 102
— — Smith, C C. (1953) J Amer med Ass 151 6

HISTOCHEMICAL OBSERVATIONS ON THE SUPRARENAL GLANDS IN CHOLERA

S N De
M.B Calcutta Ph.D Lond D T.M.
PROFESSOR OF PATHOLOGY

K P Sengupta
M B Calcutta
CURATOR, PATHOLOGICAL MUSEUM

N C Ganguli
M.B Calcutta
RESEARCH ASSISTANT *

DEPARTMENT OF PATHOLOGY NILRATAN SIRCAR MEDICAL COLLEGE, CALCUTTA

Cholera, a disease characterised by loss of fluid lowered blood volume shock and anoxia appears to be an ideal condition for the study of Selye s (1950) alarm reaction in man However very little is known about the activity of the suprarenal glands in cholera

Rogers (1921) citing Nearne considered the high tolerance of cholera patients to adrenaline as an indication of suprarenal dysfunction.

Chatterjee (1930) studied the suprarenal glands from some cases of cholera and thought the congestion of boundary zone to be related to the extreme shock of the first stage of the disease

Lahiri (1946) treated a few cases with total suprarenal cortical extract and noted some improvement of the vascular tone

We have in the past searched in vain for any significant morphological change in the suprarenals in cholera by ordinary staining methods The recent paper by Stoner et al (1953) prompted us to try their histochemical methods on our cholera materials. A preliminary report of our findings was read at the fifth annual meeting of the Indian Association of Pathologists

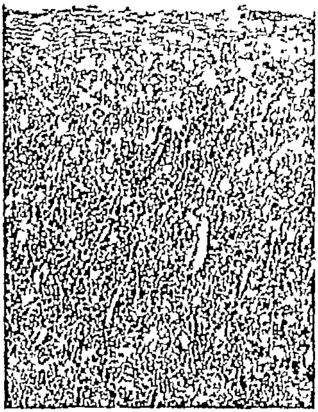


Fig. 2—Suprarenal gland in cholera showing complete depletion of sudanophil material (no black stain) Details as in fig 1

Materials and Methods

We studied eleven pairs of suprarenal glands from bacteriologically positive cases of cholera fatal within 48 hours after onset in the stage of shock Ten pairs of glands from patients dying within 15 minutes of injuries from street or railway accidents served as controls None of the patients was aged less than 10 years and the controls showed no gross pathological changes except those of their injuries The necropsies were done 24–48 hours after death on bodies kept in the cold chamber Five frozen sections from different blocks of each gland were prepared for the detection of neutral fat by staining with Sudan IV, of cholesterol with digitonin seen by polarised light and of ketosteroids with 2 4 dinitrophenylhydrazine No attempt was made to ascertain the weights of the glands the thicknesses of different zones or the cell-size

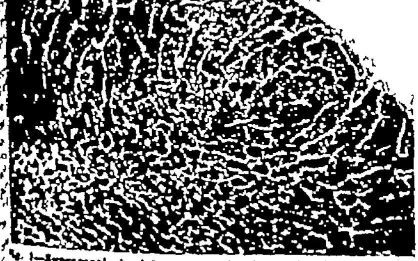


Fig. 1—Suprarenal gland from control dying within 15 minutes of a severe street injury Black stain shows sudanophilia. Frozen section 20 µ thick. (Sudan IV × 70.)

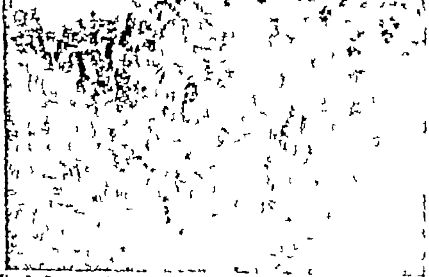


Fig 3—Suprarenal gland in cholera, showing small sudanophil islets retained. Details as in fig 1

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* Under the auspices of the Indian Council of Medical Research

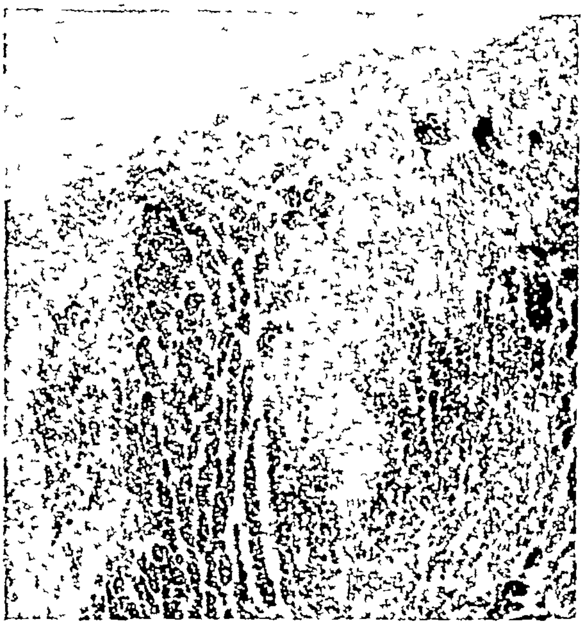


Fig 4—Patchy disappearance of sudanophil material in suprarenal gland in cholera. Details as in fig 1

Results

In four cases there was evidence of complete depletion of neutral fat from all the zones (figs 1 and 2) Only an occasional cholesterol crystal could be made out here and there Staining for ketosteroid showed a faint pale yellow coloration

In five cases neutral fat was seen to have disappeared in patches of varying extent—either wide areas still retained it, or wider areas had only small islands of it left here and there (figs 3 and 4) In one case loss of neutral fat was confined to the zona glomerulosa (fig 5) This patient received only $1^{1}/_{2}$ pints of saline solution before he died, in contrast to 4–38 pints received by other patients in 1–3 days In all these cases ketosteroid and cholesterol showed patchy distribution, but evidence of depletion of cholesterol was much more striking (figs 6 and 7)

In the 11th case all the zones retained sudanophil material while cholesterol crystals were confined to the zona glomerulosa only (fig 8)

One constant finding was that, whereas the neutral fat in the control glands appeared large and globular, that seen in cholera was always smaller and granular (figs 9 and 10)

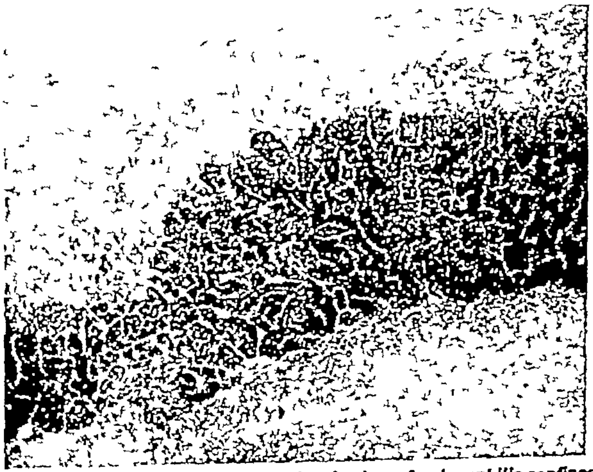


Fig 5—Suprarenal gland in cholera, showing loss of sudanophilia confined zona glomerulosa. Details as in fig 1

Discussion

This histochemical evidence of depletion of lipoid material has generally been thought to be associated with increased liberation of cortical hormone under various conditions Selye (1950) has described similar changes in his experiments on animals with non-specific alarm reaction and has related them to increased activity of the suprarenal glands under stimulation of the adrenocorticotropic hormone of the hypophysis Histochemical reactions have recently been used to investigate the functional state of the gland, but there is no agreement about their specificity Particular importance has been attached to the cholesterol content and its relative distribution An inverse correlation between cholesterol content and secretory activity of the gland has been well established by using stimuli of varying intensity and duration Sayers (1950) regards cholesterol as the precursor of cortical hormone, large stores being held in the suprarenal glands in readiness for emergency periods requiring enhanced synthesis of the hormone We have not estimated the cholesterol content of the glands but have attempted to form an idea from the above mentioned histochemical test, and there is good evidence that it tends to disappear in cholera Staining for ketosteroids may give an idea of the relative amount of the finished hormone available at the moment, but the significance of sudanophil material is not clear. A correlation between change in these lipoids has not always been possible, and Sayers (1950) thinks it is due to slight differences in technique We have, however, found a broadly parallel change in these three materials, although sometimes traces of cholesterol were left when neutral fat and ketosteroid had disappeared, or no cholesterol could be seen in the zona fasciculata, where sudanophil material still persisted Depletion of steroids has, however, been often greater than that of sudanophil material Ayres et al (1951) noted the same in acute infections

In one case the zona glomerulosa was depleted of all lipoids, and in another this zone alone showed crystal

Fig 6—Birefringent crystals of digitonin cholesterol seen in polarised light suprarenal gland from control. Frozen section 25 μ. (× 70)

Fig 7—Well marked loss of birefringent crystals from suprarenal gland in cholera. Details as in fig 6.

cholesterol. The former patient received only 1½ nts of saline solution during his short stay in the spital, and the latter received 24 pints in 46 hours It tempting to think that the *zonal picture in the two* ses was caused by hyponatræmia in the former and pernatræmia in the latter It should, however, be membered that the blood sodium level was not timated in any of these cases that only two such cases ere observed and that the question of zonal autonomy ill remains an enigma (Sayers 1950), so it will be rash draw any conclusion *from this observation*

The over-all picture seen in cholera suggests that the uprarenal glands play an active rôle in cholera by nhanced synthesis of its hormonal products This oncept finds support in another recent observation in his laboratory (De et al. 1955) on the hæmatological hanges in untreated cases of cholera Cholera is not ssociated with *suppuration or emigration of leucocytes* nywhere into the tissues yet the blood shows a leucocytosis which is much more than can be explained by simple hæmoconcentration At the same time there are neutrophilia lymphopenia, and eosinopenia Not only are the eosinophils diminished but in many cases they eem to disappear altogether from the peripheral blood. All these *facts are generally regarded* today as convincing evidence of increased suprarenal cortical activity As regards the relation of *Vibrio choleræ* or its products o these various changes, similar blood changes have been found in our vibrio negative cases Besides, no sign of necrosis or hæmorrhage has been seen in the suprarenal glands of cholera patients. These facts suggest that all the *changes in the blood and in the suprarenal glands form* part of a non-specific response on the part of the body to the associated dehydration shock and anoxia

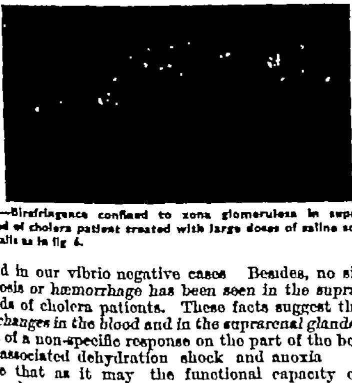


Fig. 8—Birefringence confined to zona glomerulosa in suprarenal gland of cholera patient treated with large doses of saline solution. Details as in fig 6.

Be that as it may the functional capacity of the adrenal cortex, judged by the histochemical techniques does not appear to be the same in all these cases of cholera at the time of death In four cases there was complete depletion of all lipoids—regarded by Stoner et al (1953) as evidence of complete exhaustion Cortical failure may *reasonably be suspected in these cases though* not proved. In the others variable amounts of lipoid are still left indicating that the glands retain some stock of basic elements for responding to further corticotropic stimulation In spite of such potent suprarenal glands, cortical hormonal deficiency may have been responsible for the fatal outcome when the failure may be located at a supra adrenal level

Sevitt (1954) used a combination of adrenaline and corticotrophin tests in fifty four cases of burns and diagnosed adrenocortical failure in five and failure of the pituitary-adrenal axis in two cases *Cortisone therapy* was indicated in the former and corticotrophin in the latter To clarify *the therapeutic implications* of our observations in cholera further investigations into the functional state of the two units of the pituitary suprarenal axis by serial blood-counts with these special methods up to the time of death will be necessary

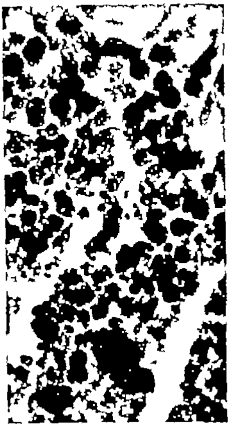


Fig. 9—Sudanophil globules in control suprarenal gland. Details as in fig 1 (× 350)

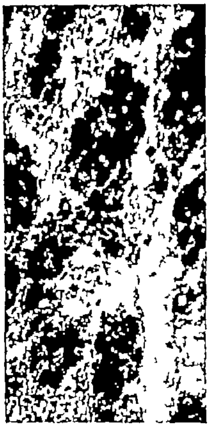


Fig 10—Sudanophil granules in suprarenal gland in cholera. Details as in fig 1

Conclusions and Summary

Evidence of various degrees of depletion of cortical lipoids suggests an active rôle of the suprarenal cortex for enhanced synthesis of its hormones in response to the stress of dehydration, shock, and anoxia of cholera

Further work to inquire into the functional state of the pituitary suprarenal system in cholera is called for

We wish to thank Dr A K. Duttagupta for permission to publish and Mr M Mazumder for the photomicrographs.

REFERENCES

Ayres, W W Firminger H. I Hamilton P K. (1951) *Milit Surg* 109 603
Chatterjee, H N (1939) *Calcutta med J* 36 165
De, S N Bose S N Mondal A (1955) To be published.
Lahiri, S C (1945) *J Indian med. Ass* 14 113
Rogers L (1921) Bowel Diseases in the Tropics. London p 198
Sayers G (1950) *Physiol Rev* 30 241
Selye, H (1950) The Physiology and Pathology of Exposure to Stress Montreal
Sevitt, S (1954) *Brit. med. J* 1, 541
Stoner H B., Whitley H J Emery J L (1953) *J Path Bact* 66, 171

CLINICAL EXPERIENCES WITH SOFT-TISSUE PLACENTOGRAPHY

Robert Percival
F.R C.S M.R C O G
OBSTETRIC SURGEON

Stanley Murray
M.D Belf F.R C.S.I., D.M.R
ASSISTANT RADIOLOGIST

THE LONDON HOSPITAL

Our object is to draw attention again to the advantages of soft tissue placentography which in our experience, has proved a safe and reliable way of establishing the position of the placenta

The work of Reid and of Whitehead on the radiological aspects of soft tissue placentography should leave no doubt as to its reliability simplicity and safety But essential for success is close collaboration between radiologist and obstetrician with interest and confidence equally distributed.

The method is valuable for several reasons. Firstly, the position of the placenta can almost always be seen or be deduced without any other examination It is not disturbing to the patient and in selected cases it may be used for outpatients Secondly it saves beds. Now that antepartum hæmorrhage is managed conservatively patients may have to stay in hospital for as long as six weeks before the fœtus is judged mature enough to risk premature delivery after examination under anæsthesia Soft tissue placentography can greatly reduce such use of valuable beds in non-toxic antepartum hæmorrhage, once placenta prævia has been excluded and bleeding has ceased the patient can safely be sent home Thirdly, it saves patients from wasting time unnecessarily in hospital No longer need a patient who has bled a little at 32 weeks, but is otherwise normal, be kept in hospital for weeks If bleeding is very slight or has stopped, it is quite easy to decide the position of the placenta within half an hour of the patient's admission It cannot be denied that up to the 34th week of pregnancy the method is not always as accurate as it is after this time, this applies to the borderline case in which the placenta appears to dip just beneath the brim, especially when it is anterior Radiography two weeks later will often show the placenta wholly above the brim, as if it had risen as the lower segment became more differentiated Finally, soft tissue placentography is a useful means of finding out whether the position of the placenta, even when in the upper segment, is responsible for a particular presentation or lie (Stevenson 1951) Moreover, it often explains why version has not been successful, and if a second attempt at version is made the dangerous placental site can be avoided

Recent Work

Chief credit for redirecting attention to this essentially simple technique must go to Reid (1949) and Whitehead (1953) The methods involving artificial-contrast media (amniography, cystography, and intravenous placentography) have been examined thoroughly by these workers, who found that they lacked simplicity and accuracy and accordingly were unsuitable for routine use Reid and Whitehead independently followed the lead of Snow and Powell (1934) and others, by making the fœtus serve as its own contrast medium and by deducing the position of the placenta from its displacement of the fœtus The need for such a technique was emphasised when Moir (1944) proved that the uterine wall, the liquor amnii, and the placenta have identical radiographic density, and that consequently no hope could be held out for ordinary soft-tissue methods in locating the placental site

In addition to the valuable radiographic density of the fœtus, use is made of another of its properties—its molecular density, which is greater than that of the fluid surrounding it The fœtus sinks to the lowest point of the amniotic cavity, and by changing the patient's position any area of the uterine wall can be examined against the outline of the fœtus

Clinical Indications for Placentography

275 cases were studied over the three-year period 1951–53 At first the patients were carefully selected, but when we became more familiar with the technique we used it more widely During the early part of the trial the method was not used by every member of the unit, so the series cannot be said to include all examples of the different clinical problems which we investigated After the first six months all patients suspected on clinical grounds of having placenta prævia were submitted to placentography The following list gives an idea of the type of case where we considered it an advantage to discover the position of the placenta

(1) Antepartum hæmorrhage, where the precise diagnosis is in doubt
(2) Unexplained displacement of the presenting part
  (a) High head
  (b) Recurrent malpresentation.
(3) Cases of (1) and (2) combined
(4) Unexplained breech presentations
(5) Unexpected failure of version
(6) Cases due for surgical induction (especially by the Drew Smythe catheter) in which the presenting part is unengaged
(7) Other indications

(1) *Antepartum hæmorrhage, where the precise diagnosis is in doubt*

This is by far the most important indication. When local causes have been excluded there remain, for practical purposes, only two conditions to differentiate—accidental hæmorrhage and placenta prævia Placentography will immediately indicate the position of the placenta There are other signs of diagnostic value when the placenta occupies the lower segment, especially in the last few weeks of pregnancy, but before this the presentation is not expected to be stable, and it is in these very cases, especially when the placenta is on the anterior wall, that physical signs are equivocal and placentography is of the greatest value

Again, bleeding thought to be caused by toxæmia may in fact be due to placenta prævia In this series the combination of toxæmia with placenta prævia was found only twice, and in neither instance was there any evidence of accidental hæmorrhage Bender (1953), on the other hand, found that toxæmic accidental hæmorrhage accounted for the bleeding in 10 of 102 cases of placenta prævia

(2) *Unexplained displacement of the presenting part*

(a) *High head*—In the last few weeks of pregnancy, if the head is high and it cannot be pushed into the pelvis, and if no other cause is found, then placentography would be helpful

(b) *Recurrent malpresentation*—The indications here are similar Stevenson (1951) has emphasised the high incidence of a completely fundal or lower-segment location of the placenta in persistent transverse lie

(3) *Case of (1) and (2) combined*

One would expect to find placenta prævia in these circumstances, yet of 38 cases of antepartum hæmorrhage associated with high head or unstable presentation only 13 had placenta prævia, in the remaining 25 the placenta was situated normally One of the criticisms levelled at radiological placental localisation has been that with placenta prævia the diagnosis can be made by abdominal examination Undoubtedly experience and an intelligent application of clinical methods will result in relatively few mistakes The patient who is known to have bled is of course admitted to hospital, but if she has not the obstetrician may become dangerously complacent unless an easy and accurate means of detecting a placenta prævia is available Moreover, the very knowledge that unexplained non engagement of the head can exist in the absence of placenta prævia may provide a ready excuse for not investigating further, and so defeat the most effective means of lowering the fœtal and maternal death rate from placenta prævia—namely, that of diagnosing it and admitting the patient to hospital before any bleeding has taken place

(4) *Unexplained breech presentations*

Stevenson (1951) has shown that the commonest site for the placenta in persistent breech is the uterine cornu and he has suggested that this causes such alteration in the shape of the uterine cavity that the fœtus is accommodated more readily as a breech In the few cases investigated we have confirmed the preponderance of the cornual position and have found placenta prævia relatively infrequently (table III)

(5) *Unexpected failure of version*

It is not uncommon to fail unexpectedly to turn a breech that has been judged suitable for version, even after it has been disengaged There are probably several reasons for this, but the most likely is that the bulk of the cornual placenta impedes the passage of the head, or so obscures the upper pole that it cannot be grasped easily. If further attempts at version are to be made, it is clearly of value to know on which side the placenta lies, so that it can be avoided It is even more important to exclude o presence of placenta prævia (unusual though it is th a breech) before making further attempts, especially anæsthesia is contemplated

) *Cases due for surgical induction in which the presenting rt is unengaged*

A not uncommon type of case is that in which there toxæmia necessitating induction but the head is not gaged though it can be pushed in In such circumstances acenta prævia can often be excluded clinically but it is ll possible for a placenta on the posterior wall to extend w enough to be disturbed by a Drew Smythe catheter bviously, it would be valuable to know that the placenta elsewhere and out of range (only then indeed should a Drew Smythe catheter be used) Bender's figures 953) relating to the cause of bleeding in placenta prævia phasise the danger of using this instrument in unsuitle cases

) *Other indications*

(a) *Previous classical cæsarean section.*—Since rupture the uterus is thought to be more common if the acenta is implanted on the uterine scar it is as well to ow the placental location in the latter weeks so that e risk may be lessened by admitting the patient to spital before term

(b) *Situation of placenta when it is prævia.*—When acenta prævia has been diagnosed by placentography e actual extent of the placenta on the anterior wall is own before operation and the technique can be anned so as to minimise maternal and fœtal blood loss. acentography may also be considered a useful prelimin y when cæsarean section is to be done under local algesia

(c) *Antepartum hæmorrhage especially before the 36th ek*—If placentography is done routinely a radiograph the fœtal skeleton is automatically available Gross ngenital abnormalities (which are more common when e placenta is prævia) may be seen and useless con rvative management for the sake of the fœtus thereby oided.

Results

PLACENTA PRÆVIA

Of 50 cases of placenta prævia (table I) 1 was missed, ving a 2% error for placenta prævia The mistake was ade early in the series and was due entirely to inexrience in interpretation Nothing similar has happened since and in cases of significant placenta prævia in the last 6 weeks of pregnancy the error should be nil Where the diagnosis is on the borderline this should be made clear in the radiological report Such cases are found mostly when placentography is undertaken too early in the last trimester, before the lower segment has become well formed In a few cases the condition is truly borderline—that is to say, the head is displaced only a little from the symphysis or promontory when the placenta extends down the anterior or posterior wall The level of the upper boundary of the lower segment is undoubtedly variable but in this technique it is assumed always to be at the pelvic brim The vagueness of this important landmark makes it all the more desirable for radiologist and obstetrician alike to be guarded in the special circumstances already mentioned before stating categorically that the placenta does not reach into the lower segment, and to be prepared to make a diagnosis of ' borderline placenta prævia

In this series the radiological diagnosis of placenta prævia was in each instance confirmed or refuted before during or after delivery by examination under anæsthesia, cæsarean section or postpartum intra-uterine palpation or by careful inspection of the placenta and membranes Neither of the last two methods is entirely satisfactory In the first place, owing to uterine retraction the placental edge either separated or still attached will often feel uncommonly low at the beginning of the third stage Where possible these findings should therefore, always be confirmed by inspection of the placenta and membranes after delivery Secondly the inspection of the placenta and membranes as a means of confirming the placental level will only be of value when the hole in the membranes has not been grossly enlarged and when the gestation sac has been expelled intact Again after measuring the distance between the placental edge and that of the hole doubt often remains as to whether the placenta did in fact reach the lower segment Where the hole was of average dimensions a distance of less than 2 in immediately placed the case in the category of placenta prævia We therefore conclude that if the diagnosis is not made before delivery in doubtful cases, the doubt will seldom be removed by any postpartum method of examination, including that of injecting the placenta via the umbilical cord with radio-opaque substances (Radio-opaque substances were not used in this series for the method was regarded as having no special merit) Finally even by examining a patient under anæsthesia before delivery it would not always be possible to feel the edge of a placenta that just reached into the lower segment, especially when the cervix is not well drawn up and when the placenta is posterior

Clinical Features

The largest group is that of antepartum hæmorrhage alone because the bleeding most commonly began before the fœtus was big enough to be regarded as unstable or unduly high The earliest diagnosis was made at 30 weeks yet strangely enough an even earlier one (at 20 weeks) was made in the next group of antepartum hæmorrhage and high head &c It might be argued that this pregnancy was not far enough advanced for the presentation to be significant yet in central placenta prævia (as this one was) the fœtus will often be found unduly high even at a comparatively early stage The difficulty of trying to rely on abdominal palpation alone to diagnose placenta prævia even when there is both antepartum hæmorrhage and a high presenting part is well shown by comparing the number of cases of antepartum hæmorrhage and high head in table I with that in table II In the placenta prævia series only 13 out of 50 (or just over a quarter) fell into the antepartum hæmorrhage and high head group whereas in the other cases there were 25 out of 84 (or slightly less than a third)—figures which are distinctly comparable.

BLE I—FEATURES OF 50 CASES OF PROVED PLACENTA PRÆVIA

marks on diagnosis :			
Correct			46
Erroneous			1
Borderline			3
w confirmed			
Cæsarean section			31
Postpartum intra-uterine palpation			7
Postpartum inspection			8
Examination under anæsthesia			10
(Some cases were confirmed by more than one method)			
ical features :	No. of cases	*Earliest diagnosed*	*Latest diagnosed*
Antepartum hæmorrhage alone	23	30th week	40th week
A.P.H. plus high head &c	13	20th week	41st week
High head or malpresentation	14	32nd week	40th week
(Of these 14 cases diagnosed before bleeding took place 4 were of 4th degree; 4 were discovered before the 36th week; and 7 had no bleeding at any time 1 of these being of 4th degree)			
Average birth-weight			6 lb. 11 oz.
tal and neonatal deaths			8 (16)
Prematurity			4
Prolapsed cord			1
Placental infarct (intra-uterine death)			1
Cord strangulation			1
Atelectasis			1

grees of placenta prævia and method of treatment

Degree	No. of cases	Average birth weight	Fœtal loss	Fœtal abnormalities	Cæsarean section	Version	Artificial rupture of membranes	Nil
1st	20	7 lb. 5 oz.	2	2	6	0	0	11
2nd	12	5 lb. 11 oz.	3	0	8	1	1	3
3rd	3	5 lb. 13 oz	1	0	3	0	0	0
4th	11	6 lb. 11 oz	2	0	14	0	0	0

There were no maternal deaths

Placenta prævia was diagnosed before any bleeding took place in 14 out of 50 cases (or nearly a third), these having been radiographed purely because of the abnormal relationship between the presenting part and the pelvic brim This suspicious sign was acted on with positive findings as early as the 32nd week in 1 instance (and there were 3 others before the 36th week), and as late as the 40th week in another In 7 patients antepartum hæmorrhage was avoided entirely, even though the average maturity at diagnosis in these patients was 35 weeks, and 1 had a 4th-degree placenta prævia No fœtus was lost, and their average birth-weight was 6 lb 11 oz

Accidental Hæmorrhage

Although pre eclamptic toxæmia was found to accompany placenta prævia on 2 occasions, there was no evidence that the bleeding was accidental In fact 1 of these patients had no bleeding at all she had a 4th-degree placenta prævia and was delivered at term (by cæsarean section) of a thriving 8 lb 3 oz baby

Examination under Anæsthesia

This was carried out on 10 patients in whom placenta prævia had been diagnosed radiographically It was done for two reasons (1) to check the radiological findings early in the series (later it was used only in borderline cases), and (2) in the lesser degree of placenta prævia, especially anterior ones, to decide on the best method of treatment Disproportion due to posterior placenta prævia is a definite indication for cæsarean section, as was emphasised by Stalworthy (1951)

Fœtal Abnormalities

The incidence of fœtal abnormalities is known to be raised in placenta prævia Macafee's (1945) figure was 3 4% In this series two developmental abnormalities were found (a hare-lip, and a meningocele) In both cases the placenta prævia was of first degree

Average Birth-weight

The conservative management of antepartum hæmorrhage, particularly when it is due to placenta prævia, is now so well established as to require no further commendation here The average birth-weight of 6 lb 11 oz in our 50 cases of placenta prævia is ample proof of the wisdom of such a policy

Fœtal and Neonatal Deaths

One of the aims in the modern management of placenta prævia is to reduce fœtal and infant loss without adding extra risk to the mother The mortality-rate of 16% in this series compares favourably with that in other reported series The average birth-weight of the fœtuses and infants lost was 5 lb 5 died after birth, the only abnormal finding being prematurity 3 were stillborn—1 from prolapse of the cord, 1 macerated from placental infarction, and 1 from the cord being tightly round the neck Table I shows that the loss was fairly evenly divided between the different degrees of placenta prævia It is unfortunate that 3 of the neonatal deaths followed cæsarean section In 6 of the patients concerned, active measures had to be undertaken to combat recurrent severe bleeding

Treatment

There were 31 cæsarean sections 14 were for 4th-degree and 3 for 3rd-degree placenta prævia Of the 8 done for 2nd degree, 1 was for a breech in an elderly primigravida, 3 were for posterior placenta prævia with apparent disproportion, and 4 were for excessive bleeding after artificial rupture of the membranes had failed to stop it In the other 2nd degree cases, bipolar version was done once when artificial rupture of the membranes did not stop the bleeding, simple artificial rupture of the membranes was also done, and in the remaining 3 cases no treatment was required 6 cæsarean sections were done for 1st-degree placenta prævia—2 for excessive bleeding, 2 for unstable presentation, 1 for associated diabetes mellitus, and 1 for prolapse of the cord

Maternal Deaths

There were no maternal deaths associated with pla prævia

Incorrectly Diagnosed and Borderline Cases

Case 1 —A para 5 with antepartum hæmorrhage, and fœtal head at 34 weeks Placentography showed a pos placenta, the head was displaced significantly, but th erroneously thought to be due possibly to clot B continued, and examination under anæsthesia show marginal placenta prævia Artificial rupture of the mem and bipolar version stopped the bleeding, but an [illegible] infant of 4 lb 3 oz was delivered, which died after [illegible] hours This case was one of the earliest in the series Th mistake was not in technique but in interpretation, and w due entirely to inexperience

Case 2 —A para 2 with antepartum hæmorrhage at [illegible] weeks Placentography revealed no significant displace of the head, and it was reported as showing "no evide placenta prævia" The patient subsequently had a nor labour with no further bleeding, but postnatal inspectio the placenta suggested that it was low lying—possibly 1 degree The infant weighed 6 lb 1 oz and did well.

Case 3 —A primigravida with a high head at term. Pla tography showed an anterior placenta and no significan placement Normal delivery took place with no bleeding, b there was a 40 oz postpartum hæmorrhage Postpar intra-uterine examination suggested that the placenta just reach into the lower segment anteriorly and was po a 1st-degree placenta prævia The infant weighed 10 lb. 1 and did well

Case 4 —A primigravida with antepartum hæmorrhage a high head at 35 weeks Placentography showed a pos placenta and there appeared to be no significant displace from the promontory to suggest that the placenta reached the lower segment The patient was examined under an thesia, and a thin edge was thought to be felt high up teriorly A 5 lb 9 oz infant was delivered spontaneous and it did well. There was no report of a postpartum inspe of the placenta and membranes to confirm this case

TABLE II—FEATURES OF 84 CASES IN WHICH ANTEPAR HÆMORRHAGE WAS NOT ASCRIBED TO PLACENTA PRÆV

Remarks on diagnosis
  Placenta prævia correctly excluded
  Placenta prævia erroneously diagnosed
  Borderline

How confirmed
  Cæsarean section
  Postpartum intra uterine palpation
  Postpartum inspection
  Examination under anæsthesia

Factors associated with antepartum hæmorrhage
  Pre-eclamptic toxæmia
  Benign hypertension
  External cephalic version
  Erosion
  Cervical polyp
  Short umbilical cord
  Unknown

Average *time in hospital* before 36th week = 11 days
Reckoned average *time saved* before 36th week = 8 days

Placental site in 65 cases of unexplained antepartum hæmorrhage
  Posterior and fundal
  Anterior
  Cornual
  Lateral

Clinical features	*No of cases*	*Earliest diagnosed*	*La dia*
Antepartum hæmorrhage alone	59	26th week	41st
Antepartum hæmorrhage, plus high head &c	25	32nd week	40th
Average birth weight			6 lb

Fœtal and neonatal deaths
  Associated factors
    External cephalic version
    Benign hypertension
    Postmaturity 6 weeks
    Prematurity
    Asphyxia

Treatment	*No of cases*	*Stillbirths neonatal d*
Normal labour	58	3
Twin labour	1	[illegible]
Breech labour	5	1
Medical induction	2	0
Surgical induction	6	0
Forceps	6	1
Examination under anæsthesia	2	0
Cæsarean section	3	0

There was 1 maternal death (due to ovarian carcinoma).

BLE III—FEATURES OF 118 CASES WITH HIGH HEAD BREECH UNSTABLE PRESENTATION &C (NO ANTEPARTUM HÆMOR RHAGE AT THE TIME OF DIAGNOSIS)

lisation of placenta	
orrect	109
ncorrect	1
orderline	3
s confirmed :	
xamination under anæsthesia	2
ostpartum intra-uterine palpation	16
ostpartum inspection	8
urgical induction	4
æsarean section	27

ociated factors :	*High head*	*Breech*	*Unstable presentation*	*Total*
lacenta prævia	6	2	6	14
ontracted pelvis	8	0	1	9
elvic tumour	6	1	0	7
ultiple pregnancy	0	0	0	0
ornual implantation	0	*4 (+1)	0	*4
ydramnios	0	0	1	1
nknown	40	8	10	58

ental position in 35 breech cases			
Anterior wall	5	Lateral wall	0
Posterior wall	0	Anterior and fundal	2
undal	0	Posterior and fundal	1
ower segment	2	Cornual	25

The only serious error in these so-called missed "cases," s made in case 1 and was due to inexperience in erpretation None of the other 3 behaved subsequently e placenta prævia cases and if in fact they were y were not of significant degree and would be correctly sed as borderline only No fœtus or mother suffered a result of the error for although the baby in case 1 d, the negative radiographic findings encouraged the ntinuation of conservative treatment to avoid pre aturity It was further bleeding that caused the birth a fragile premature infant

ANTEPARTUM HÆMORRHAGE NOT DUE TO PLACENTA PRÆVIA

There were 84 cases of antepartum hæmorrhage not to placenta prævia (table II) *In 82 a correct diagnosis* s made by radiography leaving 2 cases incorrectly gnosed 1 was a borderline case at the 39th week, d little time was wasted by *the patient in hospital.* e other, unfortunately spent four weeks in hospital ecessarily, through an error due to inexperience in chnique Of these 84 cases the absence *of placenta* evia was confirmed in 45 (table II) All the other cases haved quite normally and gave no indication of low plantation

use of Antepartum Hæmorrhage

In only 3 patients were there signs of toxæmia, and in h instance examination of the placenta after delivery ongly supported a diagnosis of toxæmic accidental morrhage It is significant that the commonest ociation was with external cephalic version The se of the bleeding was not found in 65 of the patients

ition of the Placenta in the Upper Segment

It was thought that non toxæmic antepartum hæmor ge might be associated with the position of the placen site A likely position would seem to be *the anterior* rine wall reaching nearly to the pelvic brim : there placental site would be vulnerable to trauma and be r enough to the cervix *for the blood to escape readily* ble III shows that the commonest site for the placenta non toxæmic antepartum hæmorrhage is, in fact the terior wall extending to the fundus the anterior ll is the next commonest

ditional Clinical Signs

As might be expected bleeding was the only abnor l feature in over two-thirds of the cases We have eady drawn attention to how often bleeding and ative displacement of the presenting part can be found ether in the absence of placenta prævia Much portance is attached to this observation for dangerous complacency or over anxious conservatism may result if the precision and safety of soft-tissue radiography is denied both to patient and clinician

Average Stay in Hospital

If by staying in hospital a patient is doing good for herself and for her fœtus then it would be wrong to suggest that she go home But there is no evidence that in the absence of *other symptoms and signs,* there is any advantage in keeping patients in hospital once placenta prævia has been excluded and once bleeding, which is usually slight, has stopped This belief deter mined our policy in this series. Even so the average stay in hospital before the 36th week was reached proved to be as much as 11 days this relatively high figure is largely explained by our having to keep in patients who bled too early for placenta prævia to be excluded radio graphically Even though in 1 instance placenta prævia was excluded correctly at the 26th week, it is unusual to be able to give a positive diagnosis before the 34th The arbitrary time of the 36th week was decided on because those who diagnose placenta prævia by passing a finger through the cervix under anæsthesia usually wait until then to do so

Reckoned Average Time Saved

The saving of 8 days in hospital seems small enough, but with many patients the bed saving is considerable Those who doubt the value of soft tissue placentography say that this aspect of the management should be dis counted ; but it is of real and practical importance both to these patients and to those who are waiting to occupy the beds.

Average Birth-weight

This was 6 lb 6 oz —lower than the reported average *for placenta prævia*

Fœtal and Neonatal Deaths

7 fœtuses and infants were lost giving a figure of 8 3%—about half that for placenta prævia 1 at least of these cases could hardly have had any connection with antepartum hæmorrhage the fœtus, said to have been 6 weeks postmature and weighing 11 lb died during and as a result of a very difficult delivery The other deaths cannot be attributed to our policy of discharging patients who had bled but in whom placenta prævia had been excluded radiographically since all the patients concerned were kept in hospital from the time of bleeding until they were delivered.

Fœtal Abnormality

No developmental abnormality was found in any *fœtus in this group*

Maternal Death

The only mother lost died some 2 months after delivery from ovarian carcinoma with pulmonary metastases

Incorrectly Diagnosed and Borderline Cases

Case 5 —An elderly primigravida with persistent breech presentation at the 34th week and a little bleeding after an attempt at version had failed. Placentography suggested posterior placenta prævia of significant degree but subsequent cæsarean section at term for the presentation revealed an anterior placenta in the upper segment This was again very *early in our series and before* we began to use the tilted lateral view in doubtful cases. A healthy [illegible] lb *10 oz.* baby was delivered. (Eighteen months later significant posterior placenta prævia was again diagnosed in this patient's second *pregnancy* at the 34th week, breech again presenting This time the tilted lateral view was taken and subsequent cæsarean section proved the diagnosis correct)

Case 6 — A para-5 with antepartum hæmorrhage and an unengaged head at the 39th week. The placentographic films were poor in quality and a full view of the uterus was not *available* A borderline posterior placenta prævia was diag nosed. Examination under anæsthesia was done but no placenta was felt (No postpartum examination or inspection of the placenta and membranes was recorded to confirm this finding) A healthy 7 lb 13 oz infant was subsequently delivered

HIGH HEAD, BREECH, OR UNSTABLE PRESENTATION, &C

The primary indication for placentography in this group (table III) was either an unduly high presenting part, or an unstable presentation suggesting the possibility of a low-lying placenta, in the absence of any other detectable cause Mostly the patients had reached the last month of pregnancy, but in some placenta prævia was suspected well before the 36th week, solely on the relationship of the presenting part to the brim As table I shows, 1 case of placenta prævia was suspected and proved by radiography as early as the 32nd week The patients who had a pelvic tumour were radiographed both to test the technique in these circumstances and to exclude the co-existence of placenta prævia Of 113 cases, radiographic localisation of the placenta was correct in 109 In only 1 case was the diagnosis said to be incorrect

Case 7 —A para 3 with an unstable presentation at 36 weeks Posterior placenta prævia was diagnosed by placentography, but near term the fit of the head threw doubt on the diagnosis, so artificial rupture of the membranes was done to stabilise the presentation When labour began, bleeding was so severe that cæsarean section was undertaken. The surgeon, however, was of the opinion that the placenta did not reach the lower segment No cause for the bleeding was suggested, and we offer no other explanation There were no signs of toxæmia, and a healthy 7 lb 2 oz infant was born

The other 3 cases were essentially borderline 1 of them, case 3, has already been discussed

Case 8 —A para 2 with a very unstable presentation at 35 weeks Placentography was reported as showing a minor degree of posterior placenta prævia There was no antepartum hæmorrhage or any departure from normal in the subsequent labour at term, when a healthy 6 lb 8 oz infant was delivered No postpartum intra uterine or placental examination was recorded This, therefore, must rank as an error in diagnosis, although it is possible that such a minor amount of placenta dipping below the brim might either have been carried up later by uterine growth, or been so slight as to cause no trouble

Case 9 —A primigravida with a high head at 39 weeks Placentography suggested a minor degree of posterior placenta prævia, because of slight forward displacement of the head and the placenta occupying the posterior wall No bleeding took place during labour, which began at term, but the head engaged slowly Delivery was uneventful Unfortunately there is no record of examination after labour

No mother or fœtus was lost as a result of these debatable errors No gross mistake was made in missing significant placenta prævia The errors, as they should be in this work, were rather those of commission than omission When there is doubt, "placenta prævia" should be diagnosed Just over half of the cases were confirmed by one or other of the usual methods In the remainder there was no departure from normal to suggest a low-lying placenta The different reasons for the ill-fitting or abnormal presenting part are shown in table III In about half no cause was found This is too high a proportion and simply means that such common conditions as multiparity, occipitoposterior, pelvic inclination, and hydramnios have not been recorded in the notes

Table III also shows the comparative rarity of breech presentation in placenta prævia or contracted pelvis and pelvic tumour on the one hand, and the significant coincidence of cornual implantation and breech presentation on the other Of the 35 cases of breech presentation investigated, the placenta occupied the cornual position in no less than 24 In our series, as in Stevenson's (1951), this position was the commonest finding associated with breech presentation, and it is the most probable cause of persistent breech presentation The placental position in the [illegible] cases is shown in table III In 1 case there was both pelvic tumour and cornual implantat but precedence has been given to the tumour as the c of the breech

Further Points

Transverse or Oblique Lie

The very essence of soft tissue placentography is t use the contrasting outline of the fœtus to show by displacement the position of the placenta Unless lie is axial, with the lower pole over the brim, the imp tant brim area cannot be examined accurately, and the obstetrician should be present in the X ray depart to correct the lie immediately before placentography

Pelvic Tumour and High Head

Obviously the diagnosis of pelvic tumour will be ma by clinical examination, but it is not by any means ea to exclude the co existence of placenta prævia clinical Even when the radiologist knows of the presence of pelvic tumour, if the placenta extends well down the posterior wall it is not always possible to be sure that some of the head displacement is not due partly to placenta prævia The same is true when the head is displaced by a rectum grossly distended by fæces The difficulty does not arise when the placenta is on the anterior wall or fundus, for the radiologist can then diagnose the cause of the displacement with confidence In practice, from the aspect of delivery, it is of no importance to distinguish between tumour and placenta prævia, because cæsarean section will be needed in both However, for safe ante natal management it is important to know of the possibility of placenta prævia

Early Diagnosis

Before about the 34th week precise diagnosis can made only when the placenta is implanted mainly arou the fundus, or mainly in the lower segment Even wh *the placenta appears to extend from the* anterior posterior walls into the pelvis, at this early stage it impossible to predict how much will remain there as t *uterus grows and the lower segment forms* Natura if a case is borderline so early it will almost certain become negative for placenta prævia at a later date wh *further placentography should be done* A correct dia nosis was made in 5 of our patients by the 30th week In 3 placenta prævia was excluded, in 2 major place prævia *was discovered, and both* subsequently need cæsarean section

Placenta Prævia and the Presenting Part

The relationship of the presenting part with the pe brim is used both clinically and radiologically to det placenta prævia, and the more experienced a clinic becomes the closer will he approach the precision placentography, yet it is only in the more extrem forms of placenta prævia that he is likely to achieve comparable degree of success Similarly, it is only wh the presenting part is deeply engaged and can be palpat readily through the fornices that placenta prævia ca be excluded as the cause of bleeding in a particul patient In between these extreme examples are fou *the majority of cases of antepartum* hæmorrhage, a clinically there must be doubt about the position of th placenta Even when the head can be engaged read at term there can still be significant placenta præv The following case is an example of this

Case 10 —A para 1 had a little vaginal bleeding at ter The head was resting in the brim and could be enga readily The placentography report stated there was signifi displacement compatible with the presence of posterior plac prævia Cæsarean section was done and a posterior mar placenta prævia was found

Radiological Technique

The technique used was essentially that described Reid (1949) and by Whitehead (1953), but we redu the number of films taken to two—an anteroposter d a standing lateral which included the whole of the erus and the pelvic inlet In some a third view was eded—the tilted lateral where the standing lateral ows apparent forward displacement Very occasionally her views may be required in cases of hydramnios

High kilo voltage (115–120 kV) is used for lateral ws. Development is cut to 3½ min to avoid over ckening of the part of the film which shows the terior wall

The patient must empty the bladder immediately fore examination If the rectum is too full of fæces e procedure may have to be repeated.

Summary

Soft tissue placentography is a practical method of ating the placental site The margin of error is siderably less than with clinical methods.

Its advantages are greatest in the conservative manage nt of antepartum hæmorrhage

In cases of major degree placenta prævia the hazards digital exploration of the lower segment can be avoided ogether Only in lesser degree or borderline placenta evia, in which the risk of severe bleeding is propor nately less, may examination under anæsthesia be eded, either for final diagnosis or treatment.

The method has proved particularly useful in patients pected of having placenta prævia before they have d.

That certain placental positions may cause persistent ech presentation has been confirmed by our observa ns No association was found between the placental e and accidental antepartum hæmorrhage

REFERENCES

r S. (1952) *J Obstet Gynæc. Brit Emp* 60 508
ler C. G H (1945) *Ibid*, 52 313
J C. (1944) *Amer J Obstet Gynec* 47 198
F (1949) *Brit J Radiol* 22 557
W., Powell C. B (1934) *Amer J Roentgenol* 31 37
orthy J (1951) *Amer J Obstet Gynec* 61 720
nson, C B (1951) *Ibid* 62 486
obead A. B (1953) *Brit J Radiol*. 26 401

TREATMENT OF ADRENOGENITAL SYNDROME

WITH CORTISONE AND ŒSTROGEN

C N Armstrong
M.D Durh F.R C.P D.P.H
PHYSICIAN ROYAL VICTORIA INFIRMARY
NEWCASTLE UPON TYNE

h cases of adrenogenital syndrome presenting female udohermaphroditism due to hyperplasia of the adrenal ıds, continuous treatment with cortisone reduces the kal masculine features and the urinary excretion 17 ketosteroids and promotes the development of inine characteristics (Wilkins et al 1950 1951 1952, Vines and Dods 1954) To obtain this result large doses of cortisone (100–200 mg daily by mouth) may have to be given, and this presents difficulties where supplies of cortisone are restricted

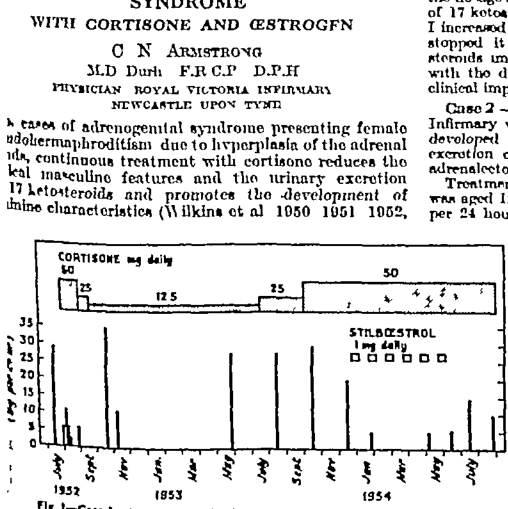


Fig 1—Case 1 : treatment and urinary excretion of 17-ketosteroids.

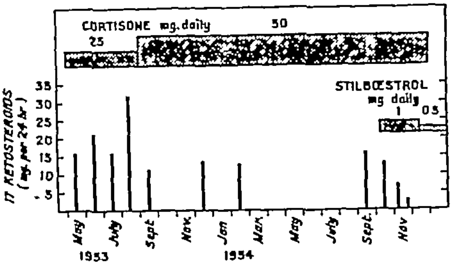


Fig. 2—Case 2 : treatment and urinary excretion of 17-ketosteroids

Treatment of such cases with œstrogen alone produces neither clinical improvement nor reduction in the excretion of 17 ketosteroids. In the following three cases, however combined therapy with œstrogen and cortisone was successful.

Case 1 —A girl aged 10 years, was admitted to the Royal Victoria Infirmary Newcastle upon Tyne with male body contours, severe hirsutism pubic hair of male distribution, undeveloped *breasts, and urinary excretion of 17 ketosteroids* 36 mg per 24 hours A congenitally large clitoris had been amputated

Laparotomy revealed uterus vagina, and ovaries Right adrenalectomy was performed but produced no improvement

Treatment with oral cortisone was begun with 50 mg daily in 1952, when the patient was 16 and the urinary excretion of 17 ketosteroids was reduced from 29·0 mg to 2 8 mg The dosage of cortisone was reduced to 25 mg and later 10 mg daily with no change in the clinical picture The excretion of 17 ketosteroids increased to 30 mg ; so the cortisone dosage was increased to 50 mg daily When the excretion of 17 ketosteroids was 21 mg under this dosage of cortisone I prescribed (for acne) 1 mg of stilbœstrol *daily for 14 days followed by 14 days without stilbœstrol,* the dosage of cortisone remaining 50 mg daily The excretion of 17 ketosteroids decreased rapidly to 4 5 mg in 24 hours I increased the dosage of stilbœstrol to 2 mg daily and then stopped it whereupon the urinary excretion of 17 keto steroids immediately began to increase (fig 1) Coincident with the decrease in excretion of 17 ketosteroids there was clinical improvement

Case 2 —*A girl aged 9 was admitted to the Royal Victoria* Infirmary with a deep voice a hypertrophied clitoris, well *developed pubic hair ; the vagina was present* Urinary excretion of 17 ketosteroids 23 6 mg per 24 hours Left adrenalectomy did not produce any clinical improvement

Treatment with cortisone was started when the patient was aged 12 and her excretion of 17 ketosteroids was 10 mg per 24 hours. The dosage was 25 mg daily and was later increased to 50 mg daily The excretion of 17 ketosteroids fluctuated somewhat but the smallest amount excreted was 11 mg in 24 hours and the girl's breasts began to develop when the excretion of 17 ketosteroids was 15 3 mg Stilbœstrol 1 mg daily was prescribed in addition to the 50 mg of cortisone daily and the excretion of 17 ketosteroids decreased to 6·8 mg *and later 2 3 mg per 24 hours (fig 2) Menstruation was also* established.

Case 3 —In this girl an enlarged clitoris was found at the age of 1 year and pubic hair began to grow at the age of 2½ years In 1953 when she was aged 14 treatment was started with oral cortisone 50 mg daily The excretion of 17 ketosteroids decreased from 23 0 mg per 24 hours to 13 2 mg *and later* to 7 8 mg but increased again to 10·5 mg The breasts began to develop and menstruation

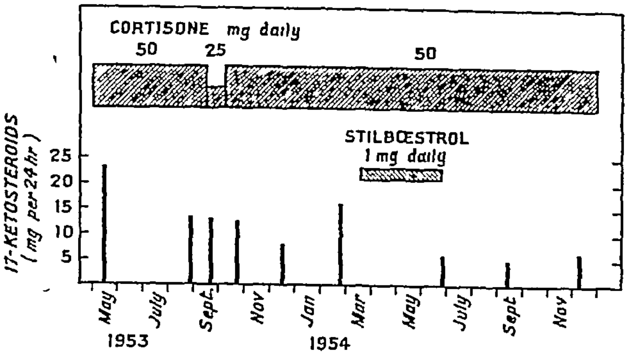


Fig 3—Case 3 : treatment and urinary excretion of 17-ketosteroids

was established With the dosage of cortisone kept at 50 mg daily stilbœstrol 1 mg daily was prescribed, and the urinary excretion of 17 ketosteroids decreased to 6 0 mg per 24 hours (fig 3) Stilbœstrol therapy had to be stopped then because of heavy menstrual bleeding

These cases show that, in the treatment of female pseudohermaphroditism, administration of œstrogen and cortisone is more effective than cortisone alone in reducing a high urinary excretion of 17-ketosteroids

REFERENCES

Vines R , Dods L (1954) *Aust Ann Med* 3 5

Wilkins L , Gardner, L I , Crigler J F et al (1952) *J clin Endocrin* 12, 257

— Lewis R. A Klein, R , Rosemberg, E (1950) *Bull Johns Hopk Hosp* 86, 249

— — — Gardner L I , Crigler J F , Rosemberg, E , Migeon C J (1951) *J clin Endocrin* 11, 1

MASSIVE BLOOD-TRANSFUSION THROUGH THE CEPHALIC VEIN

E G Dolton
M B Lond , F R C S
THORACIC SURGEON, ROYAL HOSPITAL, WOLVERHAMPTON

Patients undergoing major thoracic surgery may need very rapid transfusion of considerable quantities of blood Cannulation of the internal saphenous vein at the ankle leads to a disappointingly slow flow In the commonly favoured lateral position this may be partly due to compression of the saphenous vein at the knee and in the thigh by the opposing limb or an intervening pillow, and also possibly the opened chest and relaxed abdominal muscles lessen the negative pressure responsible for normal systemic venous flow Needling of an arm vein is more effective but often unsatisfactory Intra arterial transfusion gives a rapid replacement of blood lost by major cardiac or vascular injury but is not easy to do, requires a special pump and expert medical su and leads to an excess of potassium in the p (Melrose and Wilson 1953)

What is wanted is a large cannula inserted into a superficial vein reasonably near the heart No the inferior vena cava is of use, but the external vein and the cephalic vein near the shoulder satisfy criteria Use of the external jugular would lead to on the neck , therefore the cephalic vein is to be I was encouraged to use this vein by Dr N H then casualty registrar to this hospital, who told had given infusions through the cephalic vein successfully in cases of burns

My assistants and I have cannulated the cephalic in over 100 cases in the past twelve months. The runs very freely, venospasm has not occurred, and pint of blood can be completely transfused within minutes without any form of pressure The vein is thin-walled, easily dilated at the site of tion, and admits an unexpectedly large cannula ease This method has proved eminently satisfactory without any complication, and I recommend it to engaged in major surgery and not blessed with assistants

The only disadvantage has been that on nine the cephalic vein has been absent from its normal tion Such patients have had small transverse taneous veins across the front of the shoulder, and I not now explore for the cephalic vein when such present

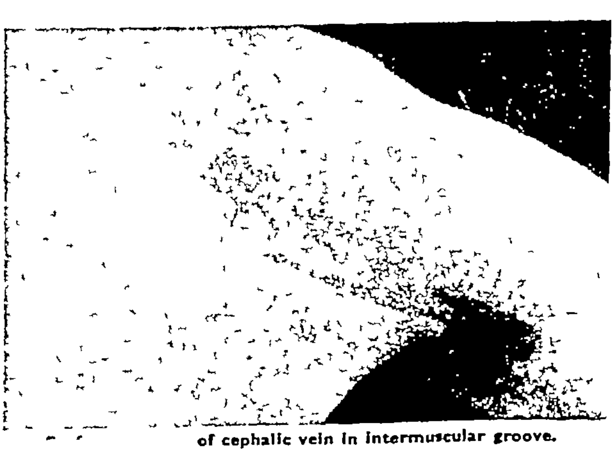
Anatomy

The cephalic vein begins on the radial side of dorsum of the hand, runs up the radial side of the and at the bend of the elbow gives off a median branch medially to join the basilic vein Thereafter travels up the outer side of the arm lateral to the muscle until it crosses the anterior aspect of the of the deltoid muscle , it next approaches from lateral side the groove between the deltoid muscle the pectoralis major muscle, and soon runs in the itself (see figure) , about two inches higher the sinks deeply into the groove and becomes difficult to by ordinary dissection No artery accompanies it. ever deepening course leads it to the coracoclav fascia, which it pierces, and it ends in the subcl vein The junction of tributary with recipient vein be guarded by valves, but these are often absent

This description is based on surgical exploration on several post-mortem dissections

Procedure

It has been found convenient to cannulate the when general anæsthesia has been induced and with patient supine The arm which will be uppermost operation is selected, because flexion and compress the lowermost arm has caused angulation of the and failure of the drip With the arm held away from side of the body at about 45° (most easily accompl by placing the hand under the upper part of the an incision 2 inches long along the lower part of deltoideopectoral groove, and extending just below beginning of that groove, will expose the vein If vein is not in the groove it will be found slightly laterally, over the deltoid muscle The vein is thin easily dilated, and in an adult takes the largest Bailey cannula , the medium Bailey cannula and normal adult Sutton cannula can usually be introd into the vein of a child aged 5–10 years After I customarily insert a distal skin stitch which holds cannula in its second loop, and a proximal skin which, passing under the vein, is left long and until after the cannula has finally been removed



of cephalic vein in intermuscular groove.

REFERENCE

Melrose, D G , Wilson, A O (1953) *Lancet*, i, 1266

THROMBOCYTOPENIC PURPURA SSOCIATED WITH OXYTETRACYCLINE THERAPY

A G BECKETT
B.M Oxf'd M.R C.P
IOR MEDICAL REGISTRAR, ROYAL FREE HOSPITAL, LONDON

A. W H. FOXELL
M.B Lond
MATOLOGIST, NORTH WESTERN GROUP LABORATORY LONDON

ALTHOUGH oxytetracycline is known occasionally to use toxic reactions in the skin and gastro intestinal act, no case of blood dyscrasia (including thrombo topenic purpura) due to this drug has been reported in is country

In a nation wide survey of 1448 cases of blood dyscrasia the United States, Welch et al (1954) report 41 cases of blood orders associated with oxytetracycline therapy including cases of thrombocytopenia in 4 of which no other drug s given. The outcome and details of these cases are not ported. Of the 409 cases of thrombocytopenia 62 were ssified as due to 'infection' and 266 as idiopathic It is refore possible that some or all of the cases associated with ytetracycline therapy should have been classified under ther of these headings.

We describe here a case of thrombocytopenic purpura ssibly due to oxytetracycline

Case-report

A man, aged 77 was admitted to hospital on Oct 19 1954 th bilateral pneumonia, which had started 10 days earlier th tiredness followed 3 days later by pain in the chest and termittent ache in the right ear For at least 10 years he had d Paget's disease of bone 3 years previously he was found have diabetes mellitus, which was subsequently treated by et alone. There was no history of any tendency to morrhage.

On admission his temperature was 99°F pulse rate 100 d respirations 28 per min. He was flushed and dyspnœic th signs of consolidation at the left base and coarse crepita tions with expiratory rhonchi at the right base He had a llapsing pulse and blood pressure 160/70 mm. Hg Paget's sease of the tibiæ was present the changes being more onounced in the right leg There was no retinopathy the ee and ankle jerks were absent but vibration sense was sent.

vestigations

Radiography of the chest showed extensive pneumonic anges in the lower zones, greater on the right side On ct 20 the hæmoglobin was 90% (13·3 g per 100 ml) and the hite cells were 9900 per c.mm. (differential count of normal stribution); the erythrocyte-sedimentation rate (E.S.R.) as 120 mm. in 1 hour (Westergren) The serum alkaline osphatase level was 9·5 King Armstrong units per 100 ml he sputum contained scanty pus cells and on culture grew *reptococcus viridans* Cultures of swabs from ear and eye re sterile

reatment and Progress

Treatment with penicillin and sulphadiazine started on the ening of admission by his private doctor was continued r 24 hours; but as there was no improvement and his ndition was serious, these drugs were stopped and he was ven a course of oxytetracycline 1·0 g initially followed by 5 g. twice daily Little or no improvement followed at first ute otitis media was diagnosed on Oct 24 and was treated ith chloramphenicol in propylene glycol which was applied to e auditory meatus on a wool wick 6 hourly for 18 hours. yringotomy was then performed under general anæsthesia nd the discharge stopped a few days later

On Oct. 26 the patient had acute cardiac failure which proved after venesection and administration of oxygen and travenous aminophylline Subsequently he was treated ith digitalis and mersalyl and had no further episodes. ecause of the severity of the illness and this episode of rdiac failure the dosage of oxytetracycline was increased 5 g 6 hourly being given for the next 6 days. This produced clinical improvement the symptoms decreasing and the temperature which had been 99–100°F falling to normal The signs in the lungs did not change however and radiography showed increased shadows in both lower zones extending into the mid zone on the left

The white-cell count, which on Oct 27 was 21 000 per c.mm (neutrophils 91%) fell to 10 000 per c.mm. 9 days later The E.S.R. was now 65 mm. in the first hour The sputum again produced a heavy growth of *Strep viridans* Oxytetracycline was continued on a reduced dosage 1 g daily in two divided doses for 8 days making a total of 26 g in 22 days.

Blood Dyscrasia

On the third day after stopping the oxytetracycline the patient had a severe epistaxis followed next day by more epistaxes and gross hæmaturia By this time he had developed extensive hæmorrhagic purpura During the next 24 hours many fresh cutaneous hæmorrhages appeared and the hæmaturia continued At this stage he had normochromic and normocytic anæmia, thought to be due to blood loss The hæmoglobin was 66% (9·8 g per 100 ml) red cells were 3 270 000 per c.mm and white cells 18,000 per c.mm (neutrophils 63%); *his platelets had decreased to 15 000 per c.mm* The bleeding time was much prolonged no evidence of cessation of bleeding occurring after 18 minutes. The prothrombin time and clotting time were normal and the Hess test was positive Next day there were further skin hæmorrhages and hæmaturia. The hæmoglobin was 63% (9·2 g per 100 ml) platelets were 11 000 per c.mm. and white cells 16 700 In the evening he started to cough up bloodstained fluid and vomited 'coffee grounds.' His general condition deteriorated rapidly and in the early hours of Nov 17 he died

The Sternal Marrow

Sternal marrow puncture was done 15 minutes after death the differential marrow count being as follows: myeloblasts 1% promyelocytes 1% neutrophil myelocytes 8% metamyelocytes 8·5% neutrophil polymorphs 51%, eosinophil polymorphs 1%, early normoblasts 4% intermediate normoblasts 6% late normoblasts 14·5% plasma cells 0·5% lymphocytes 4% and monocytes 0·5% The myeloid/erythroid ratio was 2·9/1 There was no evidence of platelet production, and only an occasional promegakaryocyte was present. No other evidence of toxic changes was seen. The development of the myeloid and erythroid series was normal apart from some increase in mature polymorphs.

Necropsy

There were numerous petechiæ in the skin of the trunk and limbs, the pericardium and endocardium, and the mucosa of the stomach small intestine colon and urinary bladder Ecchymoses were present in the pelves of the kidneys and in the leptomeninges over the left frontal and parietal lobes of the brain The lungs showed organising fibrinous pleurisy and gangrenous pneumonia with abscesses up to 2 cm. in diameter in the lower lobe of the left lung An older unresolved pneumonia, with abscesses up to 1 cm in diameter in the lower lobe of the right lung and œdema and congestion of the remainder of the lungs were also found The spleen showed subacute septic changes. Pus was present in the right middle ear The neck and upper half of the shaft of the right femur and the sternum contained red marrow

Discussion

Thrombocytopenia is occasionally associated with septicæmia but throughout his illness our patient did not show any clinical evidence of this and it seems improbable that the purpura was due to septicæmia He had suppurative pneumonia, diabetes mellitus and Paget's disease of the bone none of which are known to produce thrombocytopenia

Sulphonamides and chloramphenicol cause thrombocytopenia on rare occasions, but we do not think they were responsible for it in this case because the sulphadiazine was given for only 24 hours to a total of 2·5 g and the bleeding did not come on until 3 weeks later Chloramphenicol was applied aurally only on three occasions in 18 hours and this local application could scarcely have had a toxic effect on the marrow

In spite of the widespread use of mercurial diuretics we have found only 3 published reports of thrombocytopenia possibly due to mercurials (Butt and Simonsen

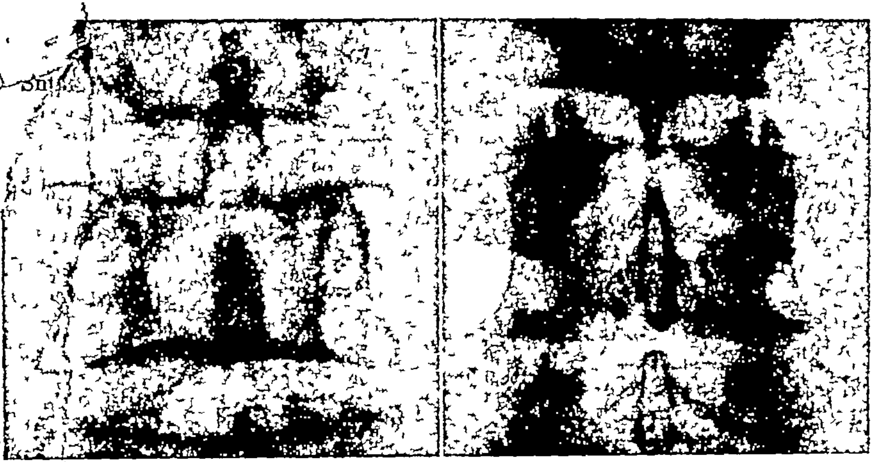


Fig 6—The normal vertebra on the right shows a fine *honeycomb* pattern, in contrast to the osteoporotic vertebra on the left which is less radio-opaque, and shows *relatively few but coarser* trabeculæ *of mainly longitudinal distribution*

stresses are greater up and down the spine *rather* than across The centra become biconcave, with increase in size in the intervertebral discs (fig 7) The centra may show denser end-plates *than normal* The condition is most marked in the spine, especially in the lumbar vertebræ There is a general deformity of the column, which shows a rounded kyphosis A kyphosis may, however, be due solely to disc degeneration There may be a wedge-shaped deformity of individual vertebræ All degrees of collapse occur sometimes the spinous processes become so close together that they develop false joints between them (Other decalcifying diseases, especially osteomalacia, produce similar X ray appearances in the spine, so it is unwise to make *the diagnosis* of osteoporosis on this one observation *alone*) It is usually stated that in osteoporosis the *pelvis may* be slightly affected, but the long bones scarcely ever and the skull almost never Actually, the other bones are affected, but less obviously so

Ghormley, Sutherland, and Pollock (1937) found that of pathological fractures arising from non-malignant conditions, one-third were due to senile osteoporosis, a cause three times as common as the next most numerous group

In patients over the age of 50 admitted to the Radcliffe Infirmary for fractured neck of femur, the condition is three times as common in women as in men It is difficult to believe that the women are submitted to more trauma than the men, and one must conclude that their bones are more brittle This belief is supported by work of Rutishauser and Dufour (1950) who examined patients who had died with fracture of the neck of the femur They cut sections of the necks of the unbroken femurs and found that these always showed characteristic changes including osteoporosis The condition is also found in the arms and legs, if the necessary predisposing factors are present and if it is sought (fig 8) These age changes also occur in compact bone as well as in cancellous bone (Amprino and Bairati 1936)

It must be admitted that the difficulties of determining the degree of osteoporosis by X ray examination are great Cobb (in Cowdry 1952) has described post-mortem chemical analyses of phalanges from patients whose hands had been radiographed during life A just-detectable X-ray difference of the dissected bone corresponded to a chemical difference of 9%, but a just detectable difference in X-ray films of the whole finger corresponded with a 25% difference in chemical analysis must be emphasised that these figures were obtained the most easily X-rayed bone in the body and in a ation where there is more bone than soft tissue Decal- spine must be even harder to detect

Similar experiments have been made by Fusi (1953) He placed complete and sliced lumbar vertebræ in 5% nitric acid, which slowly removed the mineral matter Radiological changes were visible when the isolated vertebræ had lost 3% of their calcium content, but he estimated that in the living subject changes begin to be recognisable only when the vertebræ have lost 60% of their calcium This is a surprising figure, but supporting evidence is provided by some experiments of Ardran (1951) He bored holes vertically through the centra of normal lumbar vertebræ taken from the post-mortem room A hole 3 mm in diameter could be seen clearly in a lateral X ray film of the isolated vertebra, but if the hole was filled with water it was entirely invisible A similar hole 14 *mm* in diameter—i e , about the size of the spinal canal—and occupying about *one* third of the diameter *of the* centrum, was naturally very obvious in *an X ray film* , but when it was filled with water it was *only just* visible as a faintly porotic area If this is so in excised vertebræ, no doubt such X-ray appearances would be even *more* difficult to detect in a vertebra in the body

One may therefore conclude that if there are X ray changes indicating osteoporosis, and particularly if there is vertebral collapse, there must be gross anatomical changes

The Strength of Bone

The mechanical strength of compact bone has been extensively studied, and a remarkable material it is. Its *tensile strength is nearly as great* as that of cast iron and its *crushing strength* three quarters of that of wrought iron (Bell, Cuthbertson, and Orr 1941) It is about three *times as strong as* wood The tensile and compression *strengths of* compact bone are about equal, an unusual *distinction among* building materials

A vertebral centrum consists essentially of a block of cancellous bone, with a very thin outer shell of compact bone and usually weakened by a surprisingly large hole on the posterior aspect for the emissary veins

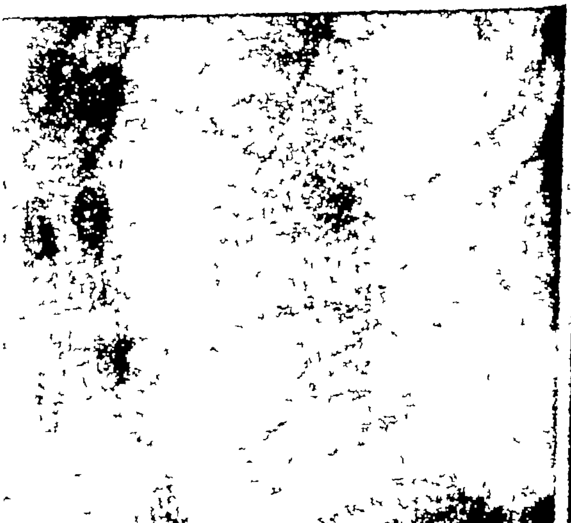
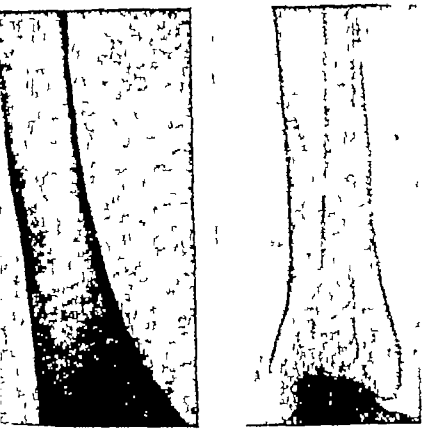


Fig 7—X ray of the thoracic spine of a woman of 73, with a long history of chyrotoxicosis and immobilisation She has a pronounced kyphosis with flattened biconcave *porotic* vertebræ



ig. 8 (same patient as fig 7)—X rays of (a) the lower end of the femur and (b) the lower end of the tibia.

have been able to find no modern reference to experiments on the strength of cancellous bone Indeed, the ly publication is that of Ward in 1838 to whose book have already referred He wrote:

> "A cubical inch of cancellous tissue was cut from the ntre of the external condyle of an adult macerated femur d subjected to gradually increasing pressure with the llowing results It sustained four hundredweight without isible alteration; sank a little on one side upon the addition the next half hundredweight and continued to yield upon ery further increase of pressure so that when the weight mounted to 6 cwt., its height was reduced to half an inch his reduction however took place entirely at the expense of e upper portion of the cube; its lower moiety which esented a much closer texture bore the whole pressure of cwt without visible alteration The weight of the cube mitted to this trial was 54 grs. troy It was placed during e experiment in the natural position with its principal res upright The side on which the cube first gave way rresponded to the outer and posterior part of the condyle d its structure was here evidently looser and more fragile an on the side which in the natural position had lain arest to the axis of the bone In Mr Rennie's experiments on e strength of woods a cubic inch of solid elm was crushed y 1284 lbs avoirdupois—about $2^1/_2$ times the weight beneath hich the cube of reticular tissue began to yield The com arison may assist the reader in forming a just estimate of the trength of the reticular tissue

I have performed some similar xperiments with the assistance f Dr J D Todd of the School f Engineering at Oxford which s equipped with appliances for sting the strength of materials riefly we found that lumbar entra from healthy subjects ithstood a pressure of 0 61–87 ton (1300–1950 lb) before ollapsing. The area of a entrum is about 2 2 sq in hich gives a strength of about 900 lb per sq in as against he 500 lb found by Ward. he difference was that his pecimen was an isolated cube f cancellous bone whereas ours ere whole centra which have thin layer of compact bone around the outside and are presumably designed specially to withstand the kind of pressure that we applied

As well as the strength of 900 lb per sq in normal centra show surprising resilience even after fracture by compression When the centrum has collapsed, if pressure be increased, the deformity becomes greater until the bone is perhaps only $^1/_4$ in thick and squashed outwards till its diameter is $2^1/_2$–3 in As soon as the pressure is released, the centrum resumes its normal shape and is sufficiently strong to resist deformity by manual pressure

Osteoporotic vertebræ are easily crushed, sometimes by trauma and sometimes spontaneously or at least by the application of little more force than the weight of the upper part of the patient's body or the slight stresses caused by the muscular movements of an old person. Centra from old or osteoporotic subjects withstand a pressure of 300 lb per sq in or less, which may seem a large figure in comparison with the normal In real life, fractures in bones are seldom produced by static forces but usually by relatively small forces applied dynamically Work by Evans Lissner and Pedersen (1948) has shown that a force of only 16 inch pounds, applied dynamically to the femur can produce deformation patterns similar to those of forces of 400–700 pounds applied statically Many forms of athletics and games must produce great stresses on the skeleton but in them fractures are relatively rare because in controlled movements the muscles are used to support the skeleton. On the other hand an unexpected fall on to the outstretched hand may produce a Colles fracture with surprisingly little violence Similarly patients with osteoporosis may fracture several vertebræ from minor but sudden trauma

Diagnosis

As I have said before osteoporosis is strictly speaking a histological diagnosis and can be made with certainty only by the morbid histologist but there are clinical features and X ray changes sufficiently well defined to justify the diagnosis at the bedside and it is an important diagnosis, because the condition is often treatable (fig 9)

In a patient over 60 years of age any pains in the trunk or legs for which there is no obvious explanation should raise in the physician's mind the possibility of osteoporosis. If the patient is a woman the chances of this being the cause are six times greater than if he is a man If there is a history of loss of height the odds in favour of the diagnosis are further increased In women special inquiry should be made about the menstrual history, the date of the menopause, and any gynæcological operations especially to ascertain whether the ovaries have been removed Questions about diet and physical activity may provide suggestive information

On examination loss of height as shown by measurement evidence of shortening of the axial skeleton a rounded kyphosis, a transverse infolding of the skin

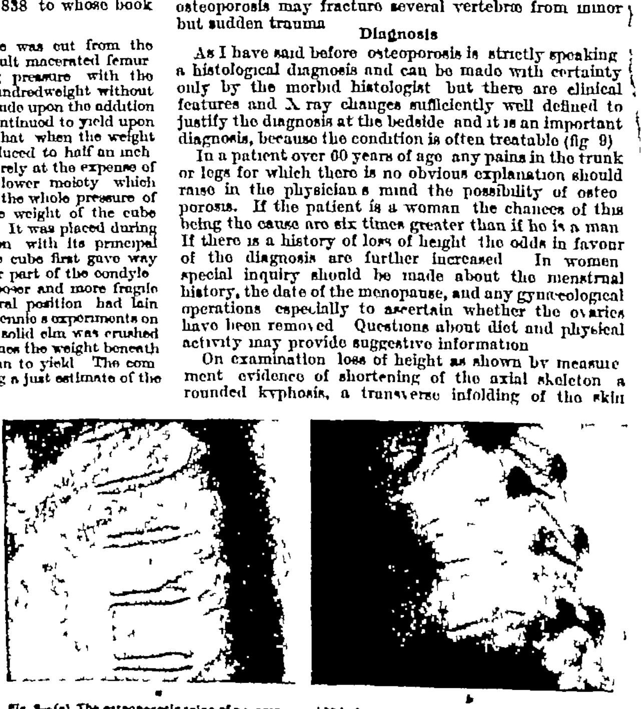


Fig 9—(a) The osteoporotic spine of a woman aged 52 before treatment. (b) The same area from the same patient (then aged 56) after 4 years treatment with calcium and vitamin D This has had no effect on the osteoporosis which has progressed and caused compression fractures

across the upper abdomen, and approximation of the lowest ribs to the pelvis are important signs The patient tends to look older than her stated age, with a lax wrinkled skin Evidence of other disease will be lacking, although the thoracic deformities make the patients unduly liable to chest infections The urine should, of course, be tested for Bence Jones protein, which strongly suggests myelomatosis *but is occasionally* found in other generalised bone diseases Sulkowitch's reagent for the quantitative estimation of calcium in the urine provides a rough screening test for the excessive calciuria of hyperparathyroidism Radiography *of the* spine and pelvis will usually reveal the characteristic changes of osteoporosis, with or without fractures If there is doubt, an X ray film of the skull (which is never affected) and some of the long bones (which are rarely affected except in very advanced cases) should provide valuable negative evidence The presence of a pseudo-fracture at once raises the question of osteomalacia, in this country usually a sequel to steatorrhœa

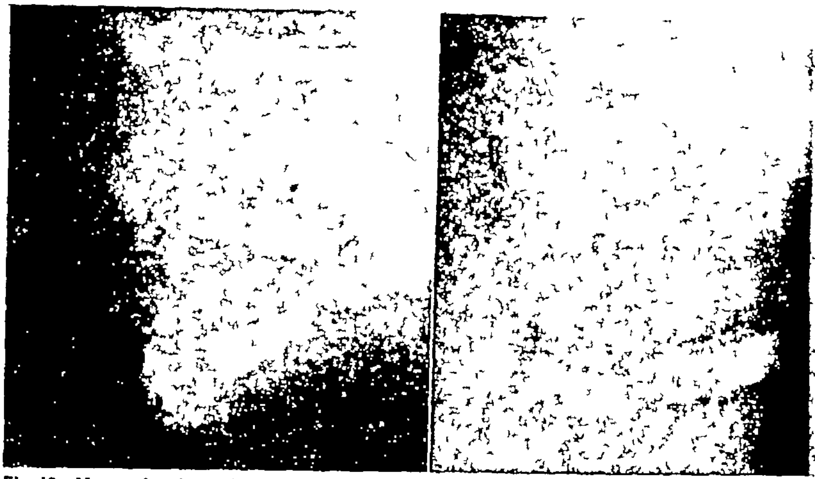


Fig 10—X rays showing radiographic improvement in osteoporosis after 2½ years hormonal therap

In osteoporosis the serum calcium and phosphorus and alkaline phosphatase are within normal limits The average total plasma-proteins are in the lower normal range and the average plasma-albumin just below the lower limit of normal Basically, *the diagnosis is made* by the exclusion of other bone diseases Bone biopsy from the iliac crest or from the dorsal spine of a lumbar vertebra is a practicable investigation (Vogt 1949, Vogt and Tonsager 1949) Lastly, it is sometimes justifiable to try a therapeutic test

Diagnostic traps are to be found in the *other diseases* that produce osteoporosis as a secondary effect Cushing's disease, acromegaly, and thyrotoxicosis usually present characteristic features which should not give rise to serious difficulties More subtle and deceptive are the osteoporotic changes of myeloma, hyperparathyroidism, the osteolytic type of Paget's disease, and so called idiopathic osteoporosis The last is a rare and puzzling variety of osteoporosis occurring in young subjects of either sex, without demonstrable endocrine defect and unresponsive to hormonal treatment

Treatment

The diagnosis of senile or postmenopausal osteoporosis made, the essentials of treatment are firstly to get the patient out of bed, if only to sit up in a chair, at the earliest possible moment Secondly, if the pains are severe, a light spinal jacket will give physical and moral support Thirdly, a high protein diet and a pint of milk a day will ensure an adequate supply of the materials from which bone is formed Last, but not least, is the hormonal treatment Opinion differs on the details, but there can be no doubt that the patient needs some preparation of male sex hormone, such as testosterone propionate 10–20 mg daily by injection, or methyl testosterone 30 mg daily by mouth Androstenediol is said to have the anabolic actions without undue masculinising effect The patient also needs a female sex hormone, such as œstradiol benzoate or dipropionate 2 mg daily by injection, or an oral preparation such as dienœstrol 1 mg daily, or æthinylœstradiol 0 1 mg daily There are satisfactory proprietary preparations containing appropriate mixtures of male and female sex hormones *Large doses are not required,* and osteoporosis is one [illegible] diseases where twice the dose of medicine *does not produce twice as good an effect, but the revers* Indeed, large doses of œstrogens inhibit bone growth Intermittent treatment will tend to prevent unpleasant side effects, and a régime of four weeks' treatment and two weeks off is often recommended Treatment should be continued for a long period, probably for not less than two years *In successful cases, the trunk pains will b* greatly improved in two weeks, and in severe bedridd cases in two months The effects of treatment are usually more pronounced in patients who have underg surgical removal of the ovaries than in those who ha had the normal gradual diminution of œstrogen activit by age

There are many cases on record of patients wi postmenopausal osteoporosis, and indeed with sen osteoporosis, who have shown great subjective improv ment on endocrine therapy and a corresponding improv ment in function, but very few cases have been report where *the X-ray appearances of the bone have be* improved Nearly all writers on the subject comment this curious fact

Cases of X ray improvement have been reported Albright and Reifenstein (1948), by Sherman (19 by Snapper (1952), and by Polishuk and Kleinh (1952), and I have seen two myself (fig 10) A poss explanation is that X-ray changes for the better are dom seen before two years' treatment and many patie are not followed up for so long a period Reifenste and Albright (1947) estimated that osteoporotic patien receiving appropriate endocrine therapy retain abo 200 mg of calcium daily If we assume that a sever osteoporotic patient has lost half the bone substance his skeleton, which is not an excessive estimate, at th rate of replacement it would take seven or eight years restore the bones to normal

Voltaire's gibe that "a physician is one who po drugs of which he knows little into a body *of which* knows less" is unfortunately still true and applies ev to endocrinology In the treatment of osteoporo chief unpleasant side effects arise from the masculinis effects of androgen therapy, which are of course m noticeable in women, who provide the majority *of t* patients *There may be coarsening of the skin,* ac hirsutism, deepening of the voice, and occasionally unseemly increase in libido Oedema of the ankles m occur from retention of electrolytes These effects seldom serious, but they are distressing to the pati They can best be prevented firstly by the use of sm *doses, secondly by intermittent treatment,* and thirdly the opposing action of œstrogens

The commonest undesired effect of œstrogen ther is uterine bleeding in women past the menopause.

possible carcinogenic effects of male and female sex hormones are a very remote danger because the doses are small and the drugs are merely replacing something which the patient is lacking

Prevalence

How common is osteoporosis? Omitting local forms such as osteoporosis of the pubic bone in prostatic disease Sudeck's atrophy osteoporosis cranii circumscripta, and the like over 800 cases have been reported (references in bibliography marked with an asterisk) The proportion of female to male patients was 6 to 1 and this is a significant ratio to which I shall refer later

Albright has described osteoporosis as the commonest bone disease likely to be encountered by the physician Priority of place must I think, be disputed by Paget's disease but there can be no doubt that both are extremely common It is interesting therefore to see how osteoporosis is dealt with in the standard British textbooks of medicine for students The following table shows the number of lines devoted to the subject in ten such textbooks

Textbook	*Date*	*Osteoporosis of any type*	*Postmenopausal osteoporosis*
A	1950	0	0
B	1950	4	0
C	1951	6	6
D	1952	0	0
E	1952	0	0
F	1953	4	4
G	1953	0	0
H	1953	0	0
I	1953	40	0
J	1954	8	0
	Total	62	10

A Personal Series

My own experience is similar to that of all those who have interested themselves in this condition The adult inpatient records of the Radcliffe Infirmary over the past fifteen years show that, of the common medical osteopathies there have been 110 patients with Paget's disease, 36 with spinal osteoporosis of one sort or another and 6 with osteomalacia (all from steatorrhœa) I have also found some osteoporotic subjects among the outpatients, and with some private patients have brought the total to 50

Of these 50 patients 43 were women and 7 men 30 were over the age of 65 and the osteoporosis was presumably senile in origin 20 were under 65 14 women and 6 men, and in the women the condition was presumably postmenopausal (fig 11)

The results of routine laboratory investigations were

	Number of observations	*Mean*
Serum-calcium	37	9 5 mg per 100 ml
Plasma-phosphorus	32	4 0 mg per 100 ml.
Plasma phosphatase	31	9 6 units
Plasma-protein	19	6 7 g per 100 ml.
Plasma-albumin	19	3 7 g per 100 ml
Blood-sedimentation rate	26	25 mm. in 1 hour

It will be seen that the serum-calcium plasma phosphorus, and plasma phosphatase are all within normal limits—a diagnostic point of importance The total plasma proteins are within the normal range but the plasma albumin is just below the generally accepted lower limit of normal (4 0 g per 100 ml) The slightly raised blood sedimentation rate is difficult to relate to the bone condition because there are so many other factors which may affect it

Apropos of the low serum-albumin levels Henneman Carter, Forbes and Dempsey (1953) tried the effect of protein administration on 4 patients with osteoporosis. There was no demonstrable effect from oral administration Daily intravenous injections of 50 g of human serum albumin for periods of from nine to thirty days produced a rise in serum albumin and considerable retention of calcium and phosphorus Henneman et al inferred, but could not prove that the treatment was a stimulus to bone formation and that serum albumin might 'actually be the transport form of bone matrix precursor'

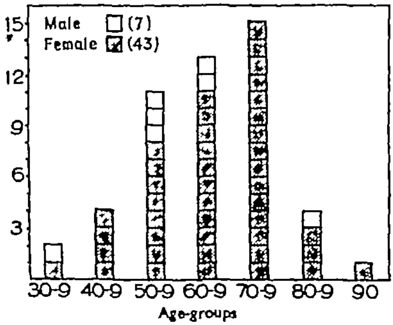


Fig 11—Age-incidence of 50 patients with spinal osteoporosis.

Of my series 37 patients were given hormones—mostly combined œstrogen and androgen therapy—but 5 had œstrogens only and 3 androgens only The follow up was adequate in 27 cases. Of these, 1 patient said that she felt worse but the remainder reported subjective improvement in varying degrees 4 patients were able to discard plaster casts, and 2, from being completely bedridden were able to get up from bed and walk about 16 patients over the age of 65 were treated with endocrine therapy and adequately followed up Of these 15 were obviously greatly improved and 1 was the patient mentioned above who felt worse

Prevention

There is no doubt that age is a common and important factor but not as has often been supposed, the only factor It is probable that a large proportion of persons over the age of 70 have some degree of osteoporosis The fact that at all ages the ratio of women to men is six to one suggests that something other than age is operative and all the evidence points to this being an endocrine factor

It is a matter of some therapeutic importance that patients with so-called senile osteoporosis respond to the appropriate treatment for so-called postmenopausal osteoporosis. The distinction between these two types is probably not only artificial but non-existent and they are really the same disease

As regards prevention there are about 7 million postmenopausal women in England and Wales, not to mention those younger who have had the ovaries removed or irradiated and over 5 million men above the age of 50 Many persons over 60 will not of course, develop osteoporosis other than the gradual and inevitable changes which will occur if they live till 70 or over But a considerable number will sustain compression *fractures* of the spine either spontaneously through extreme osteoporosis or through injuries occurring on top of moderate osteoporosis and some will become bedridden and crippled A number will sustain fractures of the *femoral* neck from trivial injuries

This formidable problem will be met if physicians surgeons and *gynæcologists* have an awareness of the existence of osteoporosis and its implications *and* realise that it is one of the few treatable chronic conditions in elderly *patients and indeed is* probably the only age change in the body that can be reversed

No-one could seriously advocate universal endocrine substitution therapy after the age *of 50* It would be administratively impossible and very costly and would carry hazards There are however some simple preven tive measures worth considering, specially by those responsible for the care of old people It will obviously be wise to encourage some physical activity, or at least to discourage undue inactivity It should not be difficult to arrange an adequate protein, calcium, and phosphorus intake—a pint of milk daily would guarantee 680 mg of calcium It would be simple to record the height of each subject annually, and to inspect the abdomen for the appearance of a transverse fold across the epigastrium Any aches or pains in the trunk for no good reason should at once call for antero posterior and lateral X rays

Patients with osteoporosis, or even patients potentially osteoporotic, should be given cortisone or corticotrophin with great caution, if possible not in large doses or for long periods (Hjorth and Dragsted 1953) In the recorded cases of osteoporosis with fractures occurring during cortisone treatment, the patient has almost always already qualified for osteoporosis by immobilisation or the postmenopausal state (Boland and Headley 1950, Teicher and Nelson 1952, Demartini, Grokoest, and Ragan 1952, Curtiss, Clark, and Herndon 1954)

Summary

I conclude by summarising the points which I consider the real essentials of these lectures

Firstly, the skeleton undergoes slow, steady resorption from all its surfaces, more apparent in cancellous than compact bone

Secondly, this process is counteracted by endocrine factors and the physical stresses and strains of use It is affected to a lesser extent by diet and age

Thirdly, osteoporosis is an extremely common condition

Fourthly, so called senile osteoporosis has an endocrine component which is treatable

It will have been obvious that these lectures have been largely a compilation from the work of others, whose original contributions to the subject I gratefully acknowledge I have received the most generous help from colleagues and friends too numerous to mention, but I must allow myself the pleasure of placing on record my particular indebtedness to Dr Alastair Robb Smith

BIBLIOGRAPHY

*Adams, M , Boothby, W M , Snell A M (1935–36) *Amer J Physiol* 114 383
Albright F (1942–43) *Harvey Lect* 38 123
— (1947*a*) *Recent Progr Hormone Res* 1, 293
— (1947*b*) *Ann intern Med* 27, 861
— Bauer, W Aub, J C (1931) *J clin Invest* 10, 187
* — Bloomberg E , Smith, P H (1940) *Trans Ass Amer Phycns*, 55, 298
* — Burnett, C H , Cope, O , Parson W (1941) *J clin Endocrin* 1, 711
— — Parson W , Reifenstein, E C Roos, A (1946) *Medicine Baltimore*, 25 390
* — Parson, W Bloomberg, E (1941) *J clin Endocrin* 1 375
— Reifenstein E C jun (1948) Parathyroid Glands and Metabolic Bone Disease Baltimore
— Smith P H Fraser R (1942) *Amer J med Sci* 204 625
* — — Richardson A M (1941) *J Amer med Ass* 116, 2465
Amprino, R , Bairati, A (1936) *Z Zellforsch* 24, 439
*Anderson, I A. (1950) *Quart J Med* 19 67
Ardran, G M. (1951) *Brit J Radiol* 24 107
Armstrong, W D (1944) *Fed Proc* 3 201
— Knowlton, M Gouze, M (1945) *Endocrinology* 36 313
Aub, J C , Bauer, W Heath C , Ropes, M. (1929) *J clin Invest* 7, 97
Baker, B L Leck L H (1946) *Amer J Physiol* 147, 522
Beadle O A (1931) *Spec Rep Ser med Res Coun Lond* no 161
Bell G H , Cuthbertson, D P , Orr, J (1941) *J Physiol* 100, 299
Bigwood E J (1952) *Ann Rev Biochem* 21, 355
*Black J R (1940) *Proc Mayo Clin* 15 619
* — Ghormley R. K , Camp J D (1941) *J Amer med Ass* 117, 2144
*Bogdonoff, M. D , Shock, N W , Parsons, J (1954) *J Gerontol* 9 262
*Boland E W , Headley, N E (1950) *J Amer med Ass* 144 365
*Burrows H J Graham G (1945) *Quart J Med* 14 147
*Coboy M C (1949) *Med Ann D C* 18 243
Cowdry E V (1952) Problems of Ageing Edited by A I Lansing Baltimore
*Curtiss P H jun. Clark, W S , Herndon, C H (1954) *J Amer med Ass* 156 467
Cuthbertson, D P (1929) *Biochem J* 23 1328
— (1930) *Ibid* 24, 1214
— (1942) *Lancet* i 433
Deitrick J E (1948) *Bull N Y Acad Med* 24 304
— W G D , Shorr E (1948) *Amer J Med* 4 3
*Demartini F , Grokoest A W , Ragan, C (1952) *J Amer med As* 149 750
*Dent R V Milne, M D , Roussak N J Steiner, G (1953) *Brit med J* ii 1082
*Dodd, K Graubarth H , Rapoport S (1950) *Pediatrics*, 6, 1
*Donaldson, I A Nassim J R (1954) *Brit med J* i 129
Drill V A (1941) *Proc Soc exp Biol*, *N Y* 48 448
Edelman I S , James A H , Baden H , Moore F D (195 *J clin Invest* 33 122
Eisenhardt, L , Thompson, K W (1938) *Yale J Biol Med* 11 5
*Elliot, M , Jackson E (1933) *Amer J Dis Child* 46 1237
Emerson, K jun Beckman W W (1945) *J clin Invest* 24 54
Evans F G Lissner, H R , Pedersen, H E (1948) *Anat Re* 101, 225
*Fairbank H A T (1939) *Brit J Surg* 27, 1
Fusi, G (1953) *Radiol Clin* 22 123
Gardner W U , Pfeiffer C A (1938) *Proc Soc. exp Biol.*, *N Y* 38 599
— — (1943) *Physiol Rev* 23 139
*Gerth (1930) *Virchows Arch* 277 311
Ghormley, R K Sutherland, C G , Pollock, G A. (1937) *J Am med Ass* 109, 2111
Gill G G (1944) *J Bone Jt Surg* 26 272
Gillespie J A (1954) *J Endocrin* 11 66
*Golden R., Abbott, H (1933) *Amer J Roentgenol* 30 641
Govaerts J Dallemagne M. J (1948) *Nature Lond* 161, 97
Greenberg D M (1939) *Ann Rev Biochem* 8 269
Halvorsen, S (1954) *Acta med scand* 149 401
Ham A W (1934) *J Amer dent Ass* 21 3
— (1952) *J Bone Jt Surg* 34A 701
— (1953) Histology Philadelphia
*Hart, G M (1950) *Geriatrics* 5, 321
Hassall A H (1849) The Microscopic Anatomy of the Hum Body in Health and Disease London 2 vols
Havers, C (1691) Osteologia Nova, or Some New Observations the Bone London
*Henneman, P H Bartter F C , Forbes A P Dempsey E F (1953) *J clin Invest* 32 574
*Hernberg, C A (1952) *Acta med scand* 143 1
Hevesy G C (1940) *Ann Rev Biochem* 9 641
— Levi, H B , Rebbe, O H (1940) *Biochem J* 34 532
Hjorth N , Dragsted P J (1953) *Acta med scand* suppl. no 2 p 33
Howard, J E Parson W , Bigham R S jun (1945) *Bull. Joh Hopk Hosp* 77 291
— — Stein K E Eisenberg H Reidt V (1941) *Ibid*, 75, 15
— Winternitz, J , Parson W , Bigham R S jun Eisenberg (1944) *Ibid* p 209
*Howard R P (1950) *Canad med Ass J* 63, 258
Huggins, C (1937) *Physiol Rev* 17 110
Ingalls N W (1931) *Amer J Anat* 48 45
Jowsey J Owen M., Vaughan, J (1953) *Brit J exp Path* 34, 6
*Junghanns H (1932) *Röntgenpraxis* 4 97
Katz J F (1953) *J Bone Jt Surg* 35A 220
*Kehoe E L , Hagan, W H (1949) *Bol Ass méd Puerto Ri* 41 80
Kenyon A T Knowlton K , Sandiford I (1944) *Ann intern M* 20, 632
— — — Koch F C , Lotwin, G (1940) *Endocrinology* 26,
*Kesson C M , Morris N McCutcheon A (1943) *Ann rheum* 6, 146
Koch J C (1917) *Amer J Anat* 21 177
Kochakian C D (1946) *Vitam & Horm* 4 256
*Labhart A , Courvoisier B (1950) *Helv med acta*, 17 475
Lacroix P (1951) The Organization of Bones Translated S Gilder London
*Lance M , Girard L Lance P (1938) *Rev Orthopéd* 25 38
Laurence, J V , Riddle O (1916) *Amer J Physiol* 41 430
Leblond C P , Wilkinson G W Bélanger L F Robichon (1950) *Amer J Anat* 86 289
*Lescher G , Robb Smith A H T (1935) *Quart J Med* 4, 2
Logan M A (1940) *Physiol Rev* 20 522
*Mackenzie, D A Janes J M (1954) *Canad med Ass J* 71 33
*Marum G J (1946) *Radiology*, 46, 220
Maxwell J P , Hu, C H , Turnbull, H M (1932) *J Path B* 35 419
*Means J H , Hertz, S , Lerman J (1937) *Ann intern Med* 11, 1
*Merklen P (1930) *Gazz Osp Clin* 57 1189
*Meulengracht E (1939) *Acta med scand* 101 138 157, 187
*Michon P , Lochard, Mme Gaussin (1948) *Rev méd Nancy*, 143
Miller, H Wilson G M (1953) *Clin Sci* 12 97
*Moehlig R C Adler, S (1947) *Surg Gynec Obstet* 64, 747
Mooser H (1921) *Virchows Arch* 229 247
*Morris N Kesson C M., Balfour B A (1943) *Quart J* 12 263
Murray P D F (1936) Bones A study of the Development Structure of the Vertebrate Skeleton Cambridge
— Huxley J S (1925) *J Anat Lond* 59 379
*Nathanson L , Lewitan A (1941) *Amer J Roentgenol* 46, 19
Neuman, W F , Weikel, J H jun (1954) The Recrystallizatio Bone Mineral University of Rochester Atomic Energy Proj
Nicolaysen R Eeg Larsen, N Malm, O J (1953) *Physiol R* 33 424
*Nordin, B E C Roper, A (1955) *Lancet*, 1, 431
*Owen E C Irving, J T , Lyall, A (1940) *Acta med scand* 103,
*Pañella-Casas M. Montoya Orta (1950) *Rev med Liège* 5,
*Plummer W A. Dunlap H F , Moore A B (1928) *Proc. Clin* 3 119
*Polishuk Z Kleinhause E M (1952) *Gynaecologia* 133, 1
Poumeau Delille G Fabiani J (1944) *C R Soc Biol* 138 238
*Ravault P P , Graber Duvernay, J Léger, G (1939) *J med Ly* 20 69
Reifenstein E C jun , Albright F (1944) *New Engl J* 231, 343
— — (1947) *J clin Invest* 26 24
Riddle O (1942) *Endocrinology* 31, 498
— McDonald, M. R (1945) *Ibid* 36, 48
— Rauch, V M Smith G C (1944) *Anat Rec* 90, 295
— Reinhart W H (1920) *Amer J Physiol* 76, 660

obinson, R. A (1952) *J Bone Jt Surg* 34A, 389
uthhauser E., Dufour, J J (1950) *Schweiz. Z allg Path.* 13 781
Schoene R. H (1952) *Ohio med J* 48 126
mon, E. F (1948) *Proc R Soc Med* 41 735
Sherman, M. (1948) *J Bone Jt Surg* 30A, 915
mons, H A. (1952) *Ibid* 34B, 275
mith, E. E., McLean, F C. (1938) *Endocrinology* 23 546
Snapper I (1952) *Med. Clin N Amer* 36 847
tevenson F H (1952) *J Bone Jt Surg* 34B 256
Strickland, B (1954) *Proc. R Soc Med* 47 341
wyman, M. L., Copleman, B (1942) *Radiology*, 39, 288
edro, C J Pomerantz, L (1942) *Arch Path* 33 305
Teicher R. Nelson, C T (1952) *J invest Derm.* 19, 205
hompson, D A W (1942) On Growth and Form. Cambridge
Vischer Poulsen, N (1953) *Geriatrics* 8 76
oot, J H (1949) *Acta med. scand* 135 291
— Tanenger A. (1949) *Ibid*, pp 231, 245
ard, F O (1838) Outlines of Human Osteology. London
eimann, J P (1950) *In* Progress in Clinical Endocrinology Edited by S. Soskin New York.
— Sicher H (1947) Bone and Bones. Fundamentals of Bone Biology London
West E. F (1954) *Med. J Aust.* 1, 84
Williams, R. H., Morgan H J (1940) *New int Clin* 2 40
illis, R. A. (1936) *Proc roy Soc* B 120, 496
yse D M. Pattee C J (1954) *Amer J Med* 17 645

HIATUS HERNIA

SURGICAL RELIEF OF REFLUX ŒSOPHAGITIS

CHARLES WELLS
M.B Lpool F.R.C.S
PROFESSOR OF SURGERY UNIVERSITY OF LIVERPOOL

J H. JOHNSTON
M.B Belf F.R.C.S F.R.C.S.I
SENIOR SURGICAL REGISTRAR, LIVERPOOL ROYAL INFIRMARY

HIATUS hernia of the sliding type is a very common condition, in which the tissues at the œsophageal hiatus of the diaphragm have relaxed and allow the cardio-œsophageal junction to become retracted into the chest This retraction unfolds the acute angle between the œsophagus and the fundus of the stomach which normally prevents reflux of the gastric contents into the œsophagus (fig 1*a*) The hernial sac may occasionally be quite large but usually it is very small—indeed scarcely more than a potential sac which can be invaginated with the finger for an inch or so (fig 1*b*) The characteristic symptoms are caused by reflux and their severity does not depend on the size of the hernia

Ætiology

The *ætiology* is not fully understood, but advancing years obesity and increased intra-abdominal pressure as in pregnancy all play a part Since the pressure within the abdomen is positive and the pressure in the chest negative it is perhaps not surprising that this hernia should appear from time to time, and its more frequent recognition in recent years may be related to dietetic and weight changes in the population Gall-stones are often found in association with hiatus hernia and may arise from common causes Hyperchlorhydria with duodenal ulceration is also a common concomitant and it is possible that in both cholelithiasis and ulcer a vagal reflex may cause muscular contractions of the œsophagus and so lead to retraction of the cardia More probably, however in duodenal ulcer it is the hyperchlorhydria which aggravates the effects of associated but unrelated reflux

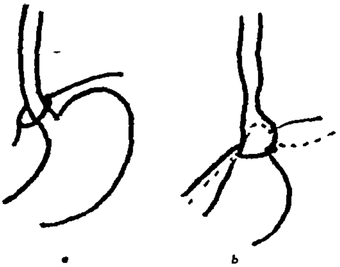


Fig 1—*a* Normal angle between œsophagus and stomach tends to obstruct gastro-œsophageal reflux; *b* retraction of cardia into thorax is followed by small sac of peritoneum (unfolding of cardia facilitates gastro-œsophageal reflux)

Symptoms and Diagnosis

The symptoms which suggest retracted cardia are heartburn (retrosternal burning pain) and acid regurgitation into the throat especially on lying down or on stooping Later there may be painful dysphagia from œsophagitis or ulceration or obstructive dysphagia from spasm or stricture The stricture may be annular from the healing of superficial lesions or may be due to dense fibrosis of the œsophagus and peri-œsophageal structures causing organic fixed shortening Secondary anæmia from steady slight bleeding is not uncommon, and sharp hæmorrhage may rarely occur One of our patients had a fatal hæmorrhage from perforation into the aorta, and in another who recovered a peri-œsophageal abscess was caused by a penetrating ulcer These severe complications are quite unusual and are more likely to arise from ulceration at the level of the hiatus in the gastric pouch of a large hernia than from the commoner inflammation or ulceration of the œsophagus itself caused by reflux. The pain of a penetrating ulcer is experienced at the level of the lower ribs, especially towards the back. It may be excited by swallowing

Investigations to confirm and assess the condition comprise radiography a search for occult blood, the estimation of gastric acidity the exclusion of other disorders (e.g duodenal ulcer and gall-stones) and œsophagoscopy The endoscopy may reveal superficial ulceration spasm or stricture formation, redness and œdema or simply an abnormal regurgitation of gastric

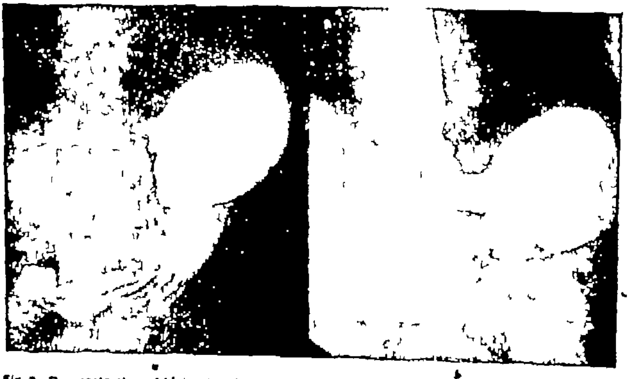


Fig 2—Demonstration of hiatus hernia: *a* with patient in head-down position diaphragm holds back gastric contents and no herniation is visible; *b* a further swallow of barium reveals herniation.

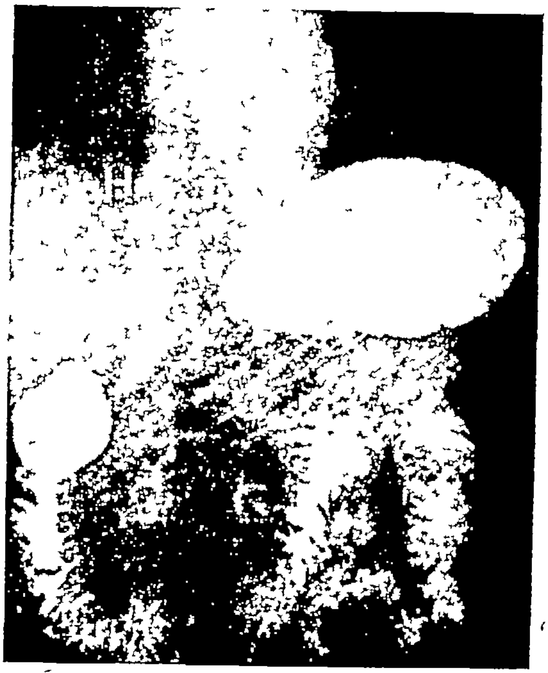


Fig 3—Typical small hiatus hernia.

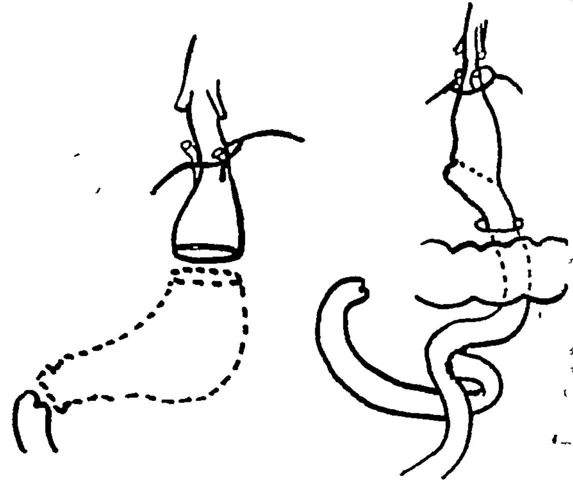


Fig 4—Scheme of operation described in text.

contents Gastric mucosa is seen sooner than is normal in some cases but not in all, since the instrument will displace the cardia downwards in the early and fully mobile case

A normal bismuth series may show retraction and incompetence of the cardia, or this may be demonstrable only with a special technique in which, after the meal, the patient, having been put in the head down position to show the fundus, is given a further bolus to swallow (fig 2) Even with the greatest care it may be difficult to distinguish with certainty between a small hiatus hernia (fig 3) and the physiological intermittent dilatation of the œsophagus, known as an epiphrenic ampulla, which is not associated with regurgitation Observation under the X-ray screen is of the greatest value and most instructive

Treatment

Non operative treatment gives a variable amount of relief Weight should be reduced, and food should not be taken for some hours before retiring, when antacids should be given as a nightcap The patient should be instructed to sleep propped well up with several pillows

Surgical Treatment — Conventional surgical treatment for those who do not get relief from non-operative measures is ordinarily directed to correction of the deformity By a thoracic approach the lower end of the œsophagus is drawn down to below the diaphragm and fixed there with sutures Reconstitution of the normal œsophago gastric angle is the essential and effective step Unfortunately most workers report a high incidence of recurrence after this operation, and in our own hands the recurrence rate has been so high that we no longer use this method

An alternative operation which we practise and advocate is based on a different principle We accept the incompetent cardia but seek to prevent regurgitation by securing rapid emptying of the stomach We also produce achlorhydria and divert the bile and pancreatic stream so that such regurgitation as may persist does no harm These desiderata are achieved by vagotomy, partial gastrectomy, and re anastomosis by the Roux-Y method (fig 4) The approach is from the abdomen

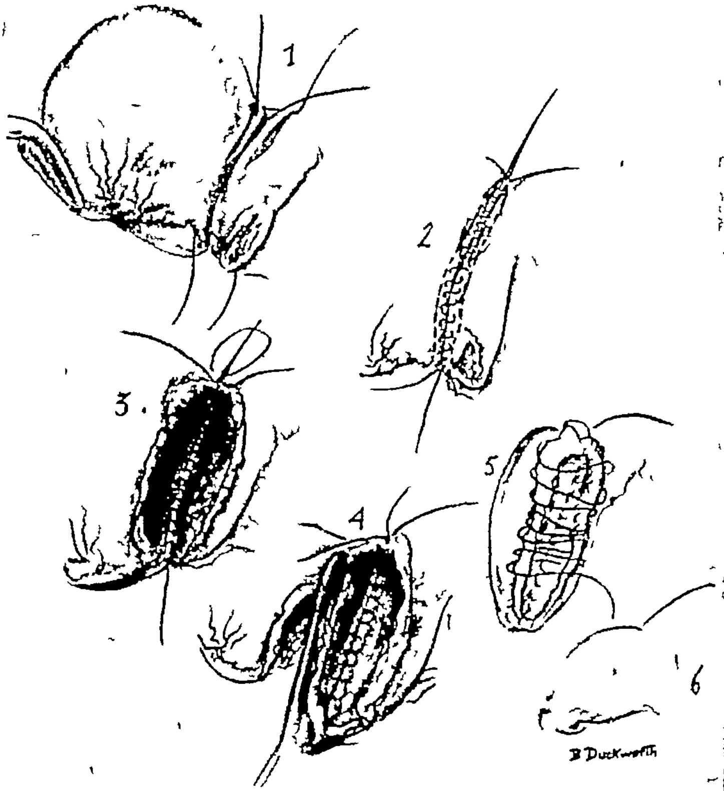


Fig 5—Gastrojejunal anastomosis : 1 start of edge-to-edge suturing at point of exit from stoma near greater curve 2 continuation of this suture line as conventional seromuscular suture and indication, by interrupted lines, of incisions into stomach and jejunum 3 posterior suture line completed and corner at open end of jejunum trimmed away; 4 distal part of stomach being cut away , 5 anterior suture line taking mucosa alone near greater curve and all coats elsewhere (cf fig 6) 6 suture-line completed

und consequently enables any associated abnormality o be given appropriate attention

The diagnosis is confirmed by palpation of the hiatus, hrough which a pouch of peritoneum can be palpated or xpelled by the examining finger If the hernia can still be educed which is usual, the left lobe of the liver is mobilised he peritoneum incised around the hiatus, and the œsophagus freed and drawn down into the abdomen for an inch or two Vagotomy is then carried out in the usual way If a completely satisfactory denervation is not achieved this fact should be carefully noted, so that in the event of pain recurring a transthoracic vagotomy may be advised If the patient is obese or if the œsophagus cannot be pulled down, vagotomy by the transthoracic approach becomes obligatory

The gastrectomy follows the usual lines. We like to conserve the gastro-epiploic arch. In hiatus hernia we do not always divide the left gastric vessel near its origin; alternatively we divide the descending branch on the lesser curve About two-thirds of the stomach is removed and the duodenum is carefully closed as usual.

The upper jejunum is then displayed and a point is selected a few inches beyond the flexure for its division Nutrient vessels are sacrificed and arcades preserved in such a way that the jejunum distal to the cut can be drawn up through the mesocolon and anastomosed to the stump of the stomach without tension The opening at the cut end of the jejunum is extended by an incision along its antimesenteric border and the resultant corners are trimmed away The anastomosis is made with great care at the point of exit at the greater curve since easy emptying of the stomach remnant is essential to success. Sometimes at this point in the anastomosis we use the edge-to-edge technique illustrated in fig 6 The mesocolon is finally fixed to the stomach proximal to and around the stoma.

The anastomosis in Y is completed about twelve inches below the stoma by bringing the biliary loop underneath and round to the left side of the vertical limb To avoid any narrowing of the jejunum carrying the food-stream (the vertical limb) the suturing is done with meticulous care in a special manner As illustrated (fig 6) the seromuscular coats are joined edge to edge with a continuous catgut stitch the loops of which are placed as delicately and as close together as possible The posterior mucosal layer is oversewn, and the stitches almost encroach on the first layer The anterior mucosal layer is made with a Connell stitch almost encroaching on the cut seromuscular coats and these are finally sutured together as in the first layer This close suturing controls hæmorrhage whilst the use of the extreme edges of the structures avoids constriction in a remarkable way

During the anastomosis it is impossible to control bleeding from the jejunal ends with the ordinary bowel clamps, but we have found that Crile's vessel-clamps on the mesenteries are excellent.

Discussion

It is twenty years since one of us performed his first gastrectomy for hiatus hernia. There was a large fixed hernia with a penetrating ulcer of the stomach at the level of the hiatus Polya gastrectomy below the level of the ulcer (Wells 1933) was undertaken as a first stage procedure It gave complete relief and no further treatment was required More recently however, we have been disappointed with the results of both the Polya gastrectomy and the Steinberg (1940) modification in the presence of retracted cardia because of the persistent

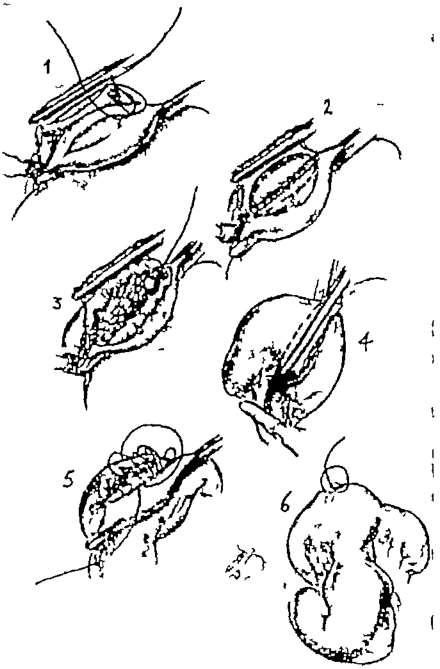


Fig 6—End-to-side jejunal anastomosis by edge-to-edge technique; 1 seromuscular coats joined; 2, incision through mucosa indicated; 3 posterior mucosal layer completed; 4 final seromuscular incision at end of afferent loop indicated; 5 anterior mucosal closure with Connell's stitch; 6 edge-to-edge seromuscular suture completed.

HIATUS HERNIA FORMER OPERATIONS, ASSOCIATED DISORDERS, AND PRESENT SYMPTOMS

Patient no	Sex	Age (yr)	Former operations	Associated abdominal disorders	Duration of follow up (mos)	Present symptoms	Weight
1	F	56	None	None	14	Sensation of fullness after meals	Gain
2	M	50	None	Duodenal ulcer	13	Eupeptic	Loss
3	F	63	None	Duodenal ulcer cholelithiasis, cholecystectomy done	13	Eupeptic	Slight loss
4	M	67	None	Duodenal ulcer	12	Eupeptic	Unchanged
5	M	29	None	None	10	Eupeptic	Gain of 1 st.
6	M	74	None	None	10	Eupeptic	Unchanged
7	F	61	None	None	4	Sensation of fullness after meals	Unchanged
8	M	49	None	None	4	Eupeptic	Unchanged
9	F	40	Heller's operation 1950 transthoracic repair of hiatus hernia 1951 Steinberg gastrectomy for recurrent hernia 1952	None	4	Eupeptic	Slight gain
10	F	45	Steinberg gastrectomy 1953	None	2	Palpitations after meals, occasional regurgitation of clear fluid	Unchanged
11	F	30	None	Cholelithiasis, cholecystectomy done	2	Eupeptic	Unchanged
12	F	64	Cholecystectomy 1940	None	[illegible]	Eupeptic	Unchanged

vomiting of bile In patients 9 and 10, who had each undergone Steinberg gastrectomy, the symptoms of œsophagitis persisted, and there was profuse regurgitation of bile on recumbency or stooping Conversion of the anastomosis to the Roux type, without disturbing the original gastrojejunal stoma, and vagotomy, have produced, in patient 9, complete relief of dyspepsia and gain in weight Patient 10 had also complained of palpitations after food, following the gastrectomy This symptom has persisted to a lesser degree after the conversion operation and, in addition, the patient has occasional reflux of clear fluid into the mouth

The cases are summarised in the accompanying table The predominant complaints in the three patients with concomitant duodenal ulcer were related to the incompetent cardia rather than the ulcer The history of the remainder conformed to a common type, and the following is typical

Case 6—A man, aged 74, was admitted to the Liverpool Royal Infirmary in August, 1953, with four years' history of burning epigastric and retrosternal pain radiating to the neck and regurgitation of acid fluid into the mouth on lying down He was often wakened at night by a choking sensation due to fluid in the throat, and there were pain and difficulty in swallowing and loss of weight Probable œsophageal carcinoma had been diagnosed in another hospital

On admission clinical examination was negative Radiography showed slight spasm in the lower œsophagus and, in the Trendelenburg position, revealed a sliding hiatus hernia with incompetence of the cardia A fractional test meal showed hyperchlorhydria Retraction of the cardia and œsophagitis were confirmed at œsophagoscopy, but, in view of the patient's age, medical treatment with diet, alkalis, and an inclined sleeping posture was advised

Progress—Seven months later the patient was readmitted with no improvement in his symptoms and requested an operation Ten months after operation he is free from dyspepsia and has returned to his work as a hairdresser

All our patients obtained complete relief from their main symptoms by operation Subsequent fractional test-meal or 'Diagnex' tests have shown achlorhydria, which suggests that vagotomy and two-thirds gastrectomy do in fact protect the Roux anastomosis from the danger of stomal and jejunal ulceration which formerly led to its abandonment in the treatment of peptic ulcer In case 8, because of difficulty in exposure, vagotomy was not performed with the gastrectomy The patient remained well until three months later, when there was a recurrence of heartburn and pain on swallowing, which was relieved by alkalis Eupepsia has been restored by transthoracic vagotomy

It was feared that the entrance of bile and pancreatic juices into the alimentary tract at a distance from the stomach might interfere with normal digestion and absorption and lead to a deficiency type of post gastrectomy syndrome, but some of the patients have in fact gained weight and in none has there been a significant loss There has been no evidence of vitamin deficiency It is too soon to be sure whether or not microcytic iron-deficiency anæmia will develop, but it is, if necessary, easily corrected (Wells and Welbourn 1951)

Summary and Conclusions

Attention is drawn to the frequency of retracted cardia and gastro œsophageal reflux as a cause of dyspepsia

The diagnosis of the condition is outlined and, for its treatment, an operation which is new in this context is described It consists in vagotomy, partial gastrectomy, and re-anastomosis by the Roux-Y method

Satisfactory early results in twelve consecutive cases are summarised

REFERENCES

Steinberg, M E (1949) *Surg Gynec Obstet* 88 453

Wells, C A (1933) *Brit med J* i 778

— Welbourn, R B (1951) *Ibid*, i, 546

THE MANAGEMENT OF CHILDREN UNDERGOING TONSILLECTOMY

PREMEDICATION WITH METHYLPENTYNOL

F R GUSTERSON

B Sc, M B Lond, F.F.A R C S

ANÆSTHETIST, WORTHING GROUP OF HOSPITALS, SUSSEX

It is estimated that every week, in Great Britain alone 1500 children undergo tonsillectomy In most cases this will be their first experience of hospital, and the responsibility for seeing that it does not cause emotional harm which may affect the child's whole life, rests largely on the anæsthetist Though much has already been written on the subject[6 14 16 17 20] it is one which should be continually reviewed in the light of new methods

Admission to Hospital

With a child of under 5 years of age, the important question is whether he has already learnt to adjust to separation from his mother by the normal process of going to school If this has not yet happened, no amount of sedation with drugs will save him from being mentally hurt by this forced separation So important did the late Sir James Spence feel this to be that he devoted much of his energies to establishing a hospital unit in which mothers had to remain in hospital with their babies It would be difficult to insist on this for tonsil cases, but much can be done even in routine hospital work to minimise the emotional trauma

So far as is practicable, each block of admissions should be of a similar age group The constant crying of the 2-year-old can be very upsetting to a 10 year-old, in addition the older boy resents being in hosp "with kids"

The mothers of all children of age groups usually admitted to children's wards should not only bring the child into hospital but should give him his first bath put on his night clothes, which could, with advantage be the child's own Many children feel more secure their own clothes The time of admission is important and should never be in the morning unless this absolutely unavoidable To put a young child to in the morning is synonymous with punishment first meal in hospital should be given by the mother aided by the nurse who will look after the child. raises a very important point The number of persons dealing with the child should be as small as possible ideally one nurse only, who will thus become temporary mother substitute

While the mother is still present, the child should meet as many as possible of the people whom he will next day, including theatre porters All these persons should be chosen for their ability to handle children there is a type of hospital porter who would frighten child out of its wits If not already done at home, would be a good time to tell the child exactly what happen the following day

One point which should be emphasised is the importance of the child's bringing into hospital some favourite toy, however shabby This is brought out very well Robertson's[28] film, in which the toy is a piece of well chewed blanket The toy will be returned the child, for the old idea of infection being transmitted in this way is no longer held This toy will naturally accompany the child to the operating theatre, which the end of a morning's list may thus look rather like scene from a Walt Disney cartoon The toy must be in the cot when the child wakes up

On the Way to the Operating-theatre

If the child is not asleep when his time comes to to the theatre he should never be made to lie down the trolley To lie flat on the back while being wheeled along corridors is very frightening The operating should be carefully timed, even when this means some inconvenience All operations on children should be done as early as possible in the day A child will tolerate the absence of his breakfast, but the absence of dinner as well, particularly if other children in the ward are having theirs, is really putting too great a strain on his control

Two more simple points are worthy of mention here The first is the old fashioned practice of making the child wear a mackintosh cap and bib for tonsillectomy With modern surgical techniques this surely is no longer necessary, and the children are much happier without them.

The other point is the wearing of face masks by the theatre staff It is most important that every person handling a child on his way to the theatre and in the anæsthetic room should have the face fully exposed Half masked faces are extremely frightening to children and it is a great help to the child to be able to recognise his ward nurse

Sedation

Many anæsthetists feel that to avoid any possible emotional upset all children of whatever age should be completely asleep before leaving the ward for the theatre This would in many ways be ideal provided that the perfect drug or combination of drugs could be found Even so the remarks in the foregoing paragraphs still apply to the time before and after the child has its actual operation and I suggest that however perfect the 'asleep in the ward' technique is some case will occur where sedation is incomplete Many think, although it is difficult to prove that in the resulting partially disorientated state a child is even more impressionable than when fully conscious This certainly applies to adults as many will remember from the early days of the use of barbiturates by mouth for premedication

Innumerable methods have already been used to ensure that every child is fully asleep before leaving the ward, and each has its enthusiastic advocates Having tried them all I have given them up one by one Personally, I feel that the rectal administration of drugs to children should be avoided except when absolutely necessary Children may not like an injection or a nasty medicine but that is an affair of the moment that a child can have explained to it. Not so with rectal interference, and the very young child is also psychologically sensitive about its rectum Hence while admitting the safety of rectal paraldehyde and the smoothness of rectal thiopentone I cannot agree that they should be used as a routine practice Furthermore I did find when using rectal paraldehyde in children some years ago that many had postoperative pyrexia and for several days were not fit to return home The disadvantages of any barbiturate (see below) are also applicable to rectal thiopentone

I have also used morphine for premedication either as morphine and atropine or as 'Omnopon' and hyoscine, using the dosage schedules advocated by various workers[8 16] I was immediately confronted with an increase in postoperative vomiting and complaints from the ward sister that quite a number of children were dangerously depressed on return to the ward, and that great difficulty was experienced in keeping their airways clear The dosage of these extremely potent drugs is small and minute errors can have serious consequences.

At present the drugs most popular for premedication are pentobarbitone ('Nembutal') and quinalbarbitone ('Seconal') Though undoubtedly satisfactory in many cases these have very grave disadvantages I have found very little to choose between them and I wonder whether it would be possible to differentiate between these two drugs by purely clinical assessment The following remarks about pentobarbitone therefore apply equally to quinalbarbitone

Barbiturates

In the first paper on pentobarbitone in this country Magill[31] wrote

> ' As with other barbiturates the variable reaction of individuals to nembutal renders the dosage by mouth and by rectum difficult to determine beforehand This is especially noticeable in children. In general, it may be stated that children are more resistant than adults and in children the variation has little to do with age or development For example, one well-developed child age 7 was fast asleep after the administration of grs. $1^1/_2$, while another child aged 6 and of small physique was quiescent but not asleep after grs. 3 had been given.

He further said that ' Irrespective of the dose or method of administration, a variable degree of restlessness was noted during the immediate post-operative period in 13 patients Five were children and their condition was controlled by potassium bromide

Waddy[30] confirmed the postoperative restlessness and in subsequent articles on these drugs the same two drawbacks of uncertainty of effect and postoperative restlessness have been mentioned[4 6 12 18 29] This still applies even if in a lesser degree, when the drug is given rectally

Postoperative restlessness is a more serious problem than this uncertainty of dosage and can be so great that a single nurse can hardly control the child A wardful of such children is in a real state of pandemonium, which can be reduced to a manageable degree only by giving morphine or one of its derivatives.

From the state of uncontrolled restlessness it is so easy to pass to that of an uncontrolled airway serious enough after any operation but liable to be extremely dangerous after an operation on tonsils and adenoids By whichever method the operation is done, blood is apt to accumulate in the upper respiratory passages Again even if the airway is not obstructed there is the very real risk that blood and mucus will be inhaled into the lungs during the state of respiratory depression which may follow the giving of morphine after a barbiturate

I was delighted to see attention drawn to this by Fraser[8] and Middleton Price[24] The situation is often made worse by ordering further morphine to control the hæmorrhage I recently had experience of such a case and at necropsy the lungs were full of inhaled blood which had without doubt been the cause of death I have indirect knowledge of other such cases which could usefully be made known and discussed Even if this complication occurs only in 1 case in 2000 it is too high a price to pay for the doubtful advantage of the child's being asleep before leaving the ward

A much less important difficulty with these barbiturate preparations is that of administration They all have an extremely unpleasant and long lasting taste and hence are supplied in capsules Nurses have developed many ingenious ways of administering these but often several mouthfuls of water are given When there has been some emotional upset during the attempt to swallow the capsules this may not be absorbed from the stomach with the result that the child vomits during the induction of anæsthesia Also in such cases the drug has not usually been absorbed and the child is still awake, thereby losing the whole purpose of this method. The drug may become absorbed later, another factor contributing to postoperative respiratory depression With these drawbacks in mind I had for some time relied on atropine alone for premedication induction usually being by intravenous thiopentone—a technique used by many others But in spite of the most careful handling about 20% of the children were obviously much upset by the visit to the theatre and yet another injection

Methylpentynol

The advent of methylpentynol therefore seemed to offer a via media between the dangers of a barbiturate and the disadvantages of no preoperative sedation All the early reports [2 7 10 11 13 22 23 25 26] of its use as a hypnotic emphasise the absence of side effects, especially respiratory depression and alteration of blood-pressure or pulse Methylpentynol was reported as having a specific effect in allaying fear and apprehension, even in doses where actual sleep was not obtained It is available commercially as a flavoured coloured elixir of 'Oblivon' (British Schering) containing 250 mg of methylpentynol per teaspoonful The flavour cannot be described as pleasant—it vaguely suggests paraldehyde—but in actual practice children very rarely complain about it

As soon as this investigation was planned, it became necessary to find some method of recording the children's reactions which would be impersonal and in no way subject to bias or prejudice It was decided to follow the work of Robertson of the Tavistock Clinic and make a film record showing children's reactions with different forms of premedication Cases were chosen at random by the camera operator from routine operating-lists This film is now available and demonstrates better than words the reactions of the children In nearly every case the child looks happy not only on going up to the theatre but also—perhaps more important still—on waking up in the ward afterwards

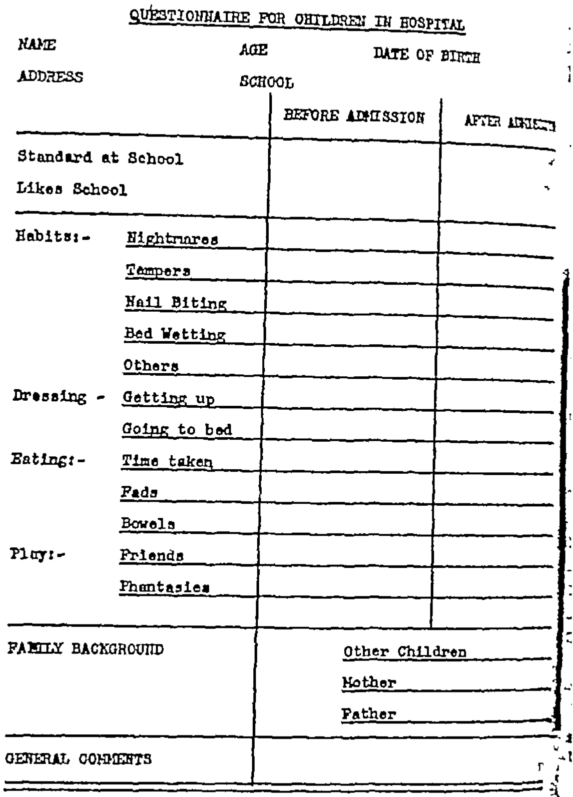
We soon found that in many cases the doses recommended by the makers had little effect We now give two teaspoonfuls for children aged 2–4 years, three teaspoonfuls for children of 4–8 (varying slightly with the build or temperament of the child), and four teaspoonfuls for children of 8–10 The methylpentynol should be given an hour before the anæsthetic, and the atropine can then be given half an hour later, when the child is much less upset by having an injection With these larger doses the children nearly all arrived in the anæsthetic room quiet and apparently unperturbed, some actually asleep though easily aroused Brown and Ellis[5] confirm the great safety margin of methylpentynol

In nearly every case anæsthesia was induced with a "sleep dose" of intravenous thiopentone This is a safe and easy procedure in a quiet and peaceful child, but the possibility of an intra-arterial injection has always to be borne in mind Attention was first drawn to this by Macintosh and Heyworth,[19] but there should be no difficulty in these cases, because the child will cry at once if the artery is touched If the child cries at all, the position of the needle must be checked, and, if there is any doubt, the injection is not continued Instead it is quite easy to induce anæsthesia with nitrous oxide without distress to the child

With this method no difficulty from vomiting in induction (Rendell[27]) has been observed, nor has there been any increase in postoperative vomiting I think the difference in my series (which now extends to more than 500 cases) is due to the fact that the methyl pentynol has been given early enough to be absorbed from the stomach

The ward immediately commented on the greatly decreased degree of postoperative restlessness in children premedicated with methylpentynol Children given no postoperative 'Nepenthe' were carefully watched and showed little restlessness, what little there was ceased in a few minutes No special control was required Absence of respiratory depression was quite obvious, and the children could keep their own airways clear even if they rolled over on to their backs This was equally true after an injection of nepenthe minim 1 per year of age With such a dose the children all remained peacefully asleep, and it is now our routine to give this injection as soon as the child shows signs of returning to consciousness

Before deciding on the value of this new method of preoperative sedation it was necessary to study it from the child's point of view A survey of these children



QUESTIONNAIRE FOR CHILDREN IN HOSPITAL

NAME AGE DATE OF BIRTH
ADDRESS SCHOOL

		BEFORE ADMISSION	AFTER ADMISS
Standard at School			
Likes School			
Habits:-	Nightmares		
	Tempers		
	Nail Biting		
	Bed Wetting		
	Others		
Dressing -	Getting up		
	Going to bed		
Eating:-	Time taken		
	Fads		
	Bowels		
Play:-	Friends		
	Phantasies		

FAMILY BACKGROUND
Other Children
Mother
Father

GENERAL COMMENTS

was therefore undertaken along the lines of th Albany Research Project[1] An experienced psychiat social worker was employed who also had a knowled of general hospital routine and an understanding children She was given the admission lists from th record department of the hospital and chose 100 cases random I did not know which cases she had visited, she did not know what anæsthetic technique had be used in any particular case Thus any possible bias opinion was eliminated. The children chosen w visited in their homes about a week before admission again several days after their return home Many of th children were visited several times in a period up to th weeks after their discharge from hospital

Several interesting factors emerged from this inve gation The first was the great advantage of a vi "by somebody from the hospital" The child's moth and the child had the whole episode explained in sim non-technical language It would be an excellent way reducing fear of hospital if this could be done in eve case, if not, perhaps a simple letter explaining th routine in hospital could be sent with the admiss note

The questionnaire is shown in the accompany figure This is quite a simple form because it was n considered advisable to make each child into a psych logical study, but all the necessary facts are includ in it

The numbers of children receiving pentobarbitone a methylpentynol were almost equal This was qu fortuitous At once it was evident that the proport of children disliking their hospital experience was equ in each case (see table)

REACTION TO STAY IN HOSPITAL

—	Received pentobarbitone	Received methylpent
No of children	51	49
Reaction favourable	40	39
Reaction unfavourable	11	10

ie "unfavourable reactors' varied in their com aints Most mentioned specifically a dislike of pricks,' while others merely mentioned that they did t like having to sleep in a room with the lights on or at they did not like the food

The number of children showing any real emotional pset was quite small in each series. Of those receiving ntobarbitone 3 showed increase of nightmares and of ose receiving methylpentynol 5 showed emotional upset ich as crying at night, and disinclination to return to hool Children showing this emotional upset were all nder 6 years old

It is therefore fair to deduce from this admittedly mall survey that there is no specific advantage from the hild's point of view in heavy preoperative sedation that btained with methylpentynol being adequate to prevent ny appreciable psychological trauma

The number of children mentioning an objection to the njection was considerable, and equal in each series This ed me to think of some method of avoiding the injection f atropine At first the atropine was dissolved in a ittle water in doses of gr $^1/_{100}$–$^1/_{50}$ according to age, nd this solution was added to the elixir This had a efinitely adverse effect on the not too pleasant taste of he elixir and in addition the children were not dry nough for comfort during induction or operation At he same time it was thought that the sedation obtained as not so good, but since secretions were not adequately ontrolled only a few cases were investigated

Hyoscine was next used in the same way in doses of r $^1/_{150}$–$^1/_{75}$ This did not affect the taste of the lixir and in every case the drying effect was satis actory In addition there was a much greater sedative ffect. Nearly every child arrived in the anaesthetic oom actually asleep, although easily aroused. In the ostoperative stage there was no restlessness and even nepenthe was given the children were quite easily roused. The ward nurses in fact commented that the hildren seemed to sleep naturally for the rest of the day ter returning to the ward although they could be oused quite easily and given a drink after which they uietly settled down and returned to sleep This modifi ation has not yet been used in many cases but so far ows great promise

It thus seems that methylpentynol, given as elixir of ethylpentynol, provides a safe and reliable premedica on for children There is no increase in emotional pset even if the children are not actually asleep on rival in the anaesthetic room Induction of anaesthesia ith a sleep dose of intravenous thiopentone gives a very mooth and pleasant induction and there is no danger of ostoperative respiratory depression The addition of oscine to the methylpentynol by mouth thereby voiding two injections, is at the moment being investi ated and shows every prospect of being successful

Summary

It is important to avoid emotional trauma in children dmitted to hospital for tonsillectomy especially when hey are under 5 years of age

Simple points in the management of children during heir stay in hospital are outlined

The disadvantages and dangers of using barbiturates r preoperative sedation are discussed

The use of methylpentynol in a flavoured elixir for reoperative sedation is described A follow up of 100 ases showed no difference between the emotional response f those children sedated with pentobarbitone and those eceiving methylpentynol Methylpentynol has a great fety margin and none of the disadvantages of the arbiturates

A sound film has been made illustrating the points the paper

I am indebted to Mr H G Downer and Mr P C Rushton hose cases these were and who performed all the operations I wish to acknowledge the very great help and coöperation I have received from the nurses of the E.N.T wards of Worthing Hospital. The children were visited by Mrs. E E Nevell, some time psychiatric social worker attached to Graylingwell Hospital The expenses of this investigation and of making the film were met by a grant from the research funds of the South West Metropolitan Regional Hospital Board. The photography was under the charge of Mr J Howard Dr R Mac Keith helped with the script of the film

REFERENCES

1 Albany Research Project (1952) Reducing Emotional Trauma in Hospitalized Children New York.
2 Allen, A W., Krongold D D (1951) *Quart Bull Sea View Hosp* 12 61
3 Anderson, S M. (1951) *Lancet* ii 965
4 Boston F K., James, N R. (1941) *Brit med J* i 5
5 Brown, I M., Ellis R. A (1955) *Ibid* i 268
6 Bullough J (1952) *Lancet* ii, 999
7 Chevalley, J Hemingway, N Moyer G., Frankhauser R McGavack T H (1952) *N Y St J Med* 52, 512
8. Eckenhoff J E (1953) *Amer J Dis Child* 86, 687
9 Fraser G A (1954) *Proc R Soc Med* 47 954
10 Gangemi, C R (1952) *Int Rec Med* 165 109
11 *Giaidroni, C. Grassi C (1952) Atti Soc lombarda Sci. Med Biol* 7 90
12 Gorham, A P (1935) *Brit med. J* ii 112
13 Hirsh H L. Orsinger W H (1952) *Amer Pract Dig Treatm* 3 23
14 Jackson, K. (1951) *Anesthesiology* 12 203
15 — Winkley R. Faust O A., Cermak, L. G (1952) *J Amer med Ass* 149 1536
16 Leigh, M. D Belton, M K (1946) *Anesthesiology* 7 611
17 Levy D M. (1945) *Amer J Dis. Child* 69 7
18 Lorber J (1950) *Brit med J* ii 21
19 Macintosh, R. R., Heyworth, P S. A. (1943) *Lancet* ii 571
20 Mac Keith R. (1953) *Ibid*, ii, 843
21 Magill, I W (1931) *Ibid* i 74
22 Malone H J., Klimkiewicz, G R. Gribetz, H J (1952) *J Pediat* 41 153
23 Margolin, S. Perlman P L. Villani F J., McGavack, T H (1951) *Science* 114 384
24 Middleton Price J (1954) *Proc R Soc Med* 47 951
25 Moravec C. L., Moravec M. E (1952) *Med Times, N Y* 80 301
26 Papa, D Villani F J Ginsberg H F (1951) *Arch. Biochem Biophys* 33, 482
27 Rendell C M. (1954) *Brit med J* i 641 *Ibid* ii 1307
28. Robertson, J (1952) A Two year-old Goes to Hospital (film) Tavistock Clinic.
29 Royal Society of Medicine (1940) *Proc R Soc Med.* 33 *83
30 Waddy F F (1933) *Brit. med J* ii 234

CHEMICALLY IDENTIFIABLE BACTERIAL RESIDUES IN LUNG LESIONS

R Consden
Ph.D Lond. A.R.I C
RESEARCH BIOCHEMIST
L E Glynn
M.D B Sc Lond. M.R C P
DIRECTOR OF THE DEPARTMENT OF PATHOLOGY
THE CANADIAN RED CROSS MEMORIAL HOSPITAL, TAPLOW,
MAIDENHEAD, BERKS

The syndrome described by Caplan (1953) in coal miners with pneumoconiosis consists in the development of radiologically characteristic pulmonary nodules in patients with concomitant rheumatoid arthritis In a community of South Wales coalminers Miall Caplan Cochrane Kilpatrick and Oldham (1953) found that more than half the men with this characteristic X ray picture also had rheumatoid arthritis compared with only 3% of those with ordinary progressive *massive fibrosis*

Because of our work on the chemistry of the subcutaneous nodules of rheumatic fever (Consden Glynn and Stanier 1953) we were invited by the South Wales investigators to study the chemistry of these various lung lesions with a view to confirming the difference between the Caplan nodule and other forms of pneumoconiotic fibrosis In the course of this work we found that in some samples the hydrolysates appeared to contain α ε diaminopimelic acid (D A P) when examined by paper chromatography Since this amino acid is not a normal constituent of mammalian tissue but is widely distributed among bacteria of various genera and species including *Mycobacterium tuberculosis* it seemed important to establish with more certainty that D A P was present especially as infection was no longer demonstrable by the usual methods of microscopy, culture, and animal inoculation. This method of detection is presented below.

Tissues Studied

(1) *A caseous nodule* obtained by biopsy from a man aged 23 was a typical caseous tuberculoma 1.5–2.0 cm. in diameter with an acellular non-fibrous necrotic centre surrounded by a zone of cellular fibrous tissue 2–3 mm. thick. Occasional foci of epithelioid and giant cells were present in this cellular zone. *No acid fast* bacilli were found despite prolonged search of several sections.

(2) *Tuberculous lung tissue* obtained by biopsy from a woman aged 28 contained several dense fibrous foci acellular *in the centre and only slightly* cellular at the periphery. The apparently necrotic centre, when stained by Gomöri's (1937) method for reticulin, revealed a dense network of fine and coarse collagen fibres with some still finer argyrophil fibrils interspersed with them. No tissue histologically characteristic of tuberculosis was seen, and no acid fast bacilli were found.

(3) *Progressive massive fibrosis*: a sample removed at necropsy from a man aged 55 consisted of jet black and fairly dense fibrous tissue about 1 cm. in diameter and surrounded by a narrow margin of emphysematous lung. The main fibrous lesion consisted of a dense central network of collagen with a surrounding fibrous capsule radiating into the surrounding lung. Similar but smaller nodules were present in the adjacent lung tissue. The acellularity of the fibrous tissue was striking.

(4) *Infective nodules* obtained at necropsy from a man aged 57 consisted of densely pigmented lung with diffuse fibrosis and some nodules up to 2 mm. in diameter formed of interlacing collagen fibres. Cellular reaction was virtually absent from the fibrous areas and the intervening lung tissue.

(5) *A Caplan nodule* obtained at biopsy from a man aged 52 was a sharply defined lesion about 1.5 cm. in diameter. Histologically the main central part of the nodule appeared structureless or faintly fibrillar when stained with hæmatoxylin and eosin, but with silver impregnation this central area was seen to be composed of a dense network of collagen fibres with finer argyrophil fibrils in the interstices. Peripherally there was a band of cellular tissue containing fibroblasts and foci of lymphocytes and histiocytes, but the cells were not in a palisade formation. The microscopic appearance lacked the characteristics of tuberculosis, and the structure of the acellular centre was quite different from that of the subcutaneous nodules of rheumatoid arthritis.

(6) *Normal lung removed* at necropsy from a male town dweller, aged 59, who died of congestive cardiac failure consisted mainly of the dark dusty surface and was used as a control of the other lung specimens.

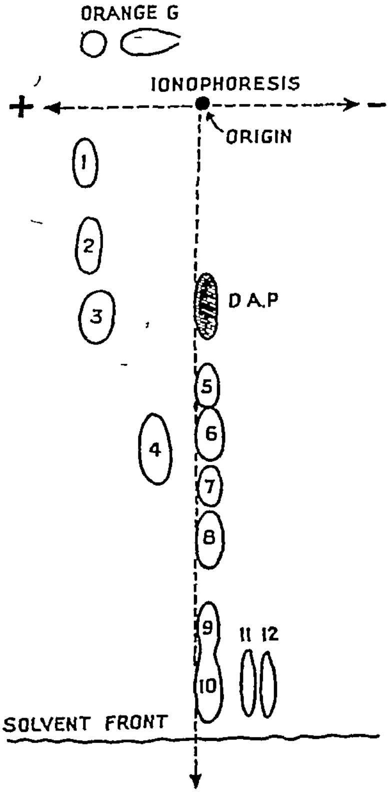
Method of Demonstrating D.A.P. in Lung Lesions

Samples of all the lung tissues were washed with 0.8% saline solution followed by distilled water, dehydrated in acetone, and autoclaved to remove collagen. Tests for D.A.P. as described below were made on the residues, since preliminary chromatography had indicated that in tissues which contained this amino acid, the bulk of it was not extracted by autoclaving. This procedure therefore has the advantage of concentrating the D.A.P.-containing constituents in the test material, because from a half to two-thirds of the organic material of the lung samples was removed by autoclaving. The residues of Caplan nodule, tuberculous lesion, and progressive massive fibrosis after autoclaving contained about one-third of the original organic matter, whereas the infective nodule and caseous nodule residues contained about one-half.

The following simple test for D.A.P. depends on a two-dimensional separation on paper by chromatography followed by ionophoresis at right angles to the direction of chromatography.

The tissue was hydrolysed with 6 N HCl at 105–110°C for 17 hours. Excess acid was removed by evaporation in vacuo. Insoluble humin was separated by centrifugation. A portion of the hydrolysate was treated with excess bromine water and stood for 5 minutes. Excess bromine and acid were removed by evacuation over KOH. The treated hydrolysate was concentrated to a suitable volume, and 5–10 µl. containing the equivalent of 0.25–0.33 mg. of protein was placed on a spot half-way across a sheet of Whatman no. 1 filter paper 24 cm. wide. Chromatography was carried out in water-saturated phenol in an atmosphere of NH_3 (produced from 0.3% NH_3 on the floor of the chamber) for 21–24 hr., by which time the solvent front had travelled about 25 cm. from the origin. The sheet was thoroughly dried and the paper below the solvent front removed. The remainder was suspended and sprayed lightly and evenly with M/20 phosphate buffer, pH 7, the spraying being done first on either side of the chromatogram and finally along the chromatogram itself. The wet sheet was then placed in position in the paper electrophoresis apparatus with the edges of the paper dipping into the electrode compartments containing M/20 phosphate buffer, pH 7. The apparatus consisted of a flat shallow 'Perspex' box designed for holding paper in a horizontal position. Before the current was applied, a drop of Orange G solution was placed above the origin to act as a control. The voltage applied was about 14 V. per cm., and the starting current 0.5 mA per cm. of width. The current was passed for 1 hour, after which the paper was removed, dried, and treated in the usual way with ninhydrin. During the ionophoresis the Orange G separates into two components (red and yellow). The faster (yellow) travels at a similar rate to *aspartic acid and hence is useful for observing progress during* the run. The resulting two dimensional separation (chromatophoretogram) is illustrated diagrammatically in the accompanying figure.

In phenol NH_3 the amino acids which would interfere with D.A.P. are glutamic acid, ethanolamine phosphoric acid, and cystine, all of which occur in animal tissues. The first two, because of their acidic nature, migrate towards the anode in an electric field. Cystine is completely oxidised by Br_2 to cysteic acid (Consden et al. 1946), which besides having a lower R_F value than D.A.P., is also acidic. D.A.P. behaves like the monoamino-monocarboxylic acids and migrates slowly towards the *cathode* because of electro endosmosis and no known amino acid of animal tissue hydrolysate would occupy the same position after two dimensional separation. Tyrosine, if present, is converted by bromine to dibromotyrosine, which migrates slowly towards the anode at pH 7 and has an R_F value in phenol similar to glycine. The basic amino-acids *migrate* towards the cathode.



Chromatophoretogram of a bromine-oxidised protein hydrolysate containing diaminopimelic acid (chromatography in phenol-NH_3, followed by ionophoresis at pH 7)

D.A.P., diaminopimelic acid. 1, cysteic acid. 2, aspartic acid. 3, glutamic acid (ethanolamine/phosphoric acid if present, would occur here). 4, dibromotyrosine. 5, serine. 6, glycine. 7, threonine. 8, alanine. 9, valine. 10, leucine &c. 11, arginine. 12, lysine.

Work at Dewey (1953) describe a method of demonstrating D.A.P., based on a similar principle but this is more laborious and time consuming than the method described above.

A number of solvents can be used for the first chromatographic separation because the interfering components of be subsequently separated by ionophoresis or converted to acidic amino-acids by oxidation However solvents which incorporate acid are a disadvantage because it is impossible subsequently to remove all the acid from the paper This increases the ionic strength of the buffer and hence causes too high a current for convenience in the ionophoretic separation Further if ethanolamine phosphoric acid were present it would only have appreciable ionophoretic mobility at pH 6 or higher (Clarke et al 1955) The acid in the paper would therefore require stronger buffer solutions to raise the pH sufficiently and this would also cause high current This could be overcome by using a lower voltage but the time of ionophoresis would be correspondingly increased The width of the sheet is not important it depends on the dimensions of the paper-electrophoresis apparatus used

Results

The lower limit of detection of D.A.P is about 0·5 µg Hydrolysed fat-extracted *M tuberculosis* by the above test showed a moderately strong D A P spot corresponding to about 5·0 µg Caseous tissue showed a spot of moderate strength (about 2·0–3·0 µg) the Caplan nodule showed a faint but quite distinct spot (about 1·0 µg), and a trace (about 0·5 µg) was found in the non caseous tuberculous lung No D.A.P was detected in the infective nodule, in the sample of progressive massive fibrosis, or in the normal lung

Discussion

D.A.P was first observed in *Corynebacterium diphtheriae* by Work (1949) and in *M tuberculosis* by Asselineau and Lederer (1950) Subsequently many investigations have shown its wide occurrence in bacteria (see Work and Dewey 1953) but it has not been demonstrated in either tissue fluids or tissue hydrolysates of mammals The ability to demonstrate D.A.P even in minute quantities in samples of lung tissue indicates heavy bacterial colonisation at some period in the evolution of the lung lesion Since the method used cannot detect less than about 0·5 µg of D.A.P the concentration of this amino-acid in the positive specimens must have exceeded 1·5–2·0 µg per mg But D A P only constitutes some 2% of the dry weight of those bacteria likely to occur in lung 1·5–2·0 µg therefore represents 5–100 µg of dry bacillus weight This is present in the residue after autoclaving and assuming that only negligible amounts of D.A.P are extracted by autoclaving evidence is thus obtained that lung lesions despite the absence of cultural or histological evidence of infection may contain identifiable bacterial residues resulting from a weight of infection amounting to at least 2·5% of the dry weight of the lesion itself

Moreover with the caseous material the strength of the D A P spot suggested that the bacterial contribution to the lesion was much higher amounting to at least 0% of the lesion These figures must not be taken as evidence that bacterial debris is actually present to this extent since the bulk of the organisms may well have been removed by the normal scavenging and enzymatic activities of the tissues On this hypothesis D A.P should be a component of the highly resistant residue of the bacteria That this is so for *M tuberculosis* has been shown by Colover and Consden (unpublished) in a chemical study of the fraction of the tubercle bacillus that is active in the experimental production of allergic encephalitis (Colover 1954) An active residue remaining after prolonged extraction with fat solvents followed by digestion with proteolytic enzymes still contained D.A.P in readily detectable amounts Some mention should be made of presence of D.A.P in the Caplan nodule and its absence in progressive massive fibrosis. Further investigation of the latter is necessary before this difference is established Prior bacterial infection might be an important factor in pathogenesis of one or both of these conditions.

Two further aspects of these results are worthy of comment

(1) The detection of bacterial debris by the presence of chemically characteristic components might well prove a useful method in the study of lesions of obscure ætiology such as sarcoidosis. The presence of either arabinose rhamnose or mycolic acid would provide further confirmation of the presence of such bacterial residues.

(2) In view of the rôle of tubercle bacilli in the experimental genesis of immunity and allergy, the persistence in the tissues of resistant bacterial fractions might be of great significance.

Summary

A method is described for identifying α ε diamino pimelic acid in some lung lesions

This amino acid was found in a caseous tuberculous nodule, a Caplan nodule, and a sample of non-caseous tuberculous lung tissue It was not found in a sample of "progressive massive fibrosis" nor in an "infective nodule"

The bacterial residues in the caseous nodule represent a weight of infection amounting to about 20% of the dry weight of the lesion

It is a pleasure to acknowledge the coöperation of Dr J Gilson, Dr W E Miall Dr D Rivers, and Dr A L Cochrane, of the Pneumoconiosis Research Unit for supplying tissues and for helpful discussion The infective nodule was provided by Prof. J Gough.

REFERENCES

Asselineau J Lederer E. (1950) *C.R Acad Sci Paris* 230 142
Caplan A (1953) *Thorax*, 8 29
Clarke H B Datta S P, Rabin, B R. (1955) *Biochem J* 59 209
Colover J (1954) *Brain*, 77 435
Consden, R. Glynn, L. E Stanier W M (1953) *Biochem. J* 55 248
— Gordon, A H Martin, A J P (1946) *Ibid* 40 580
Gomöri G (1937) *Amer J Path.* 13 993
Miall, W E. Caplan A Cochrane A L Kilpatrick, G S., Oldham P D (1953) *Brit med. J* ii, 1231
Work, E. (1949) *Biochim. biophys Acta* 3 394
— Dewey D L (1953) *J gen Microbiol* 9 394

SIMPLIFIED OPERATIVE ROUTINE FOR CARCINOMATOUS OBSTRUCTION OF COLON

B N Brooke
M D Birm. M Chir Camb F.R C.S
READER IN SURGERY UNIVERSITY OF BIRMINGHAM

FOR the treatment of acute colonic obstruction due to neoplasm it has been usual either to do the Paul-Mikulicz operation or to relieve obstruction with a colostomy later resect the lesion and finally close the colostomy Though the Paul Mikulicz method is [illegible] and only requires a second operation for closure of the colostomy it is unsuitable for the purpose of eliminating neoplasm since there is inadequate [illegible] the lymphatic field By the three stage [illegible] temporary colostomy is made as far [illegible] lesion as is practicable, in order to [illegible] adequate resection later; but at the [illegible] the temporary colostomy tends to [illegible] the abdomen and thus the area [illegible]

When obstruction [illegible]

phase of acute obstruction if the two stage procedure is planned It is to draw attention to the value of this method that the following three cases are reported

Case-reports

Case 1 —A woman, aged 70, was admitted on Feb 22, 1954, to the Queen Elizabeth Hospital with acute obstruction of the colon Laparotomy next morning revealed a mobile growth of the rectosigmoid A loop colostomy was constructed in the left iliac fossa as close to the lesion as possible After operation an infected hæmatoma formed in the wound Sixteen days after admission the abdomen was reopened through a low left paramedian incision, thus avoiding the previous site on the right side It was confirmed that the neoplasm of the rectosigmoid was at an early stage , no glands were palpable, and so anterior resection was undertaken The colostomy was detached from the abdominal wall and withdrawn into the abdominal cavity From that moment it was possible to do an anterior resection in the usual manner removing the growth within the pelvis after mobilising the upper rectum and ligating the superior hæmorrhoidal vessels , end to end anastomosis between the mobilised portion of the descending colon and the rectum at the level of the pelvic peritoneal reflexion was a simple matter after removing the sigmoid and rectosigmoid, which contained both growth and colostomy The operation was completed by suture of the laparotomy and colostomy wounds, the latter being drained Recovery was uneventful, and the patient returned home two weeks after the second operation

Case 2 was similar to case 1 as regards site of the neoplasm, but the technique of removal was somewhat different A man, aged 53, was admitted on March 24, 1954, with intestinal obstruction due to a growth found at laparotomy to be adjacent to the brim of the true pelvis The sigmoid loop was long , at the lowest possible site a colostomy was formed in the left iliac fossa After this operation the sigmoid tended to prolapse through the colostomy incision Ten days later the abdomen was reopened through the lower left paramedian incision Because of the bulk of colon exteriorised as the result of prolapse at the colostomy, it was decided to perform the dissection through the paramedian incision but deliver the resected portion through the colostomy wound, so as to avoid contamination which might result from returning the prolapsed portion and the colostomy to the abdomen The splenic flexure was mobilised, and since it was impossible to dissect in the lower part of the left paracolic gutter, the left colonic vessels were ligated at their origin from the medial side, and special care was necessary to avoid injuring the ureter An anterior resection was done with end to end anastomosis between the upper descending colon and the rectum The colostomy and the neoplasm were excised together in the length of colon removed through the colostomy incision The paracolic gutter was drained through the wound in the left iliac fossa which was repaired Convalescence was smooth and the patient returned home twelve days after operation

In **Case 3**, a woman aged 61, the lesion was at the splenic flexure The preliminary laparatomy was done through a lower left paramedian approach , and the colostomy, placed as far to the left in the transverse colon as possible was brought out above the level of the umbilicus through a left trans rectal incision Fourteen days later the left paramedian incision was reopened and was continued upwards to include the colostomy wound and detach the colostomy An excellent exposure was thus obtained, and left hemicolectomy was done with end to end anastomosis of the right transverse colon to the lower sigmoid The paracolic gutter was drained through a stab incision in the flank, and corrugated rubber was placed at the site of the pre-existing colostomy The patient had an undisturbed convalescence and was discharged twelve days later

Management before resection in all cases has included colostomy washouts , and by mouth for three days streptomycin 1 g twice daily, alternatively oxytetracycline 250 mg six hourly, or phthalylsulphathiazole 2 g thrice daily, with the same drug instilled as a suspension into the distal loop of the colostomy At operation it has been found best to tie a dry swab over the colostomy and to make no attempt to close its opening with sutures, since this tends to be ineffective and promote bleeding and thus the possible spread of contaminants In the first case oxytetracycline, and in the second case strepto-mycin, was instilled around the area of dissection and anastomosis before closing the peritoneum This was done because of the wound infection complicating the one, and the prolapse increasing the possibility of contamination in the other , no local application of this sort was made in the third patient Case 1 was given oxytetracycline after operation because pus from the previous incision was encountered on reopening the abdomen No drugs of this sort were given to cases 2 and 3 after operation, and routine chemotherapy is avoided at this stage since these drugs are better kept in reserve for possible complications

The neoplasm itself has always been covered at an early stage with a surgeon's mask, the strings of which are tied tightly around the bowel above and below the lesion to prevent exfoliated malignant cells from spreading to the site of anastomosis, where they may be implanted (Cole 1952) while the mask itself prevents direct exfoliation and implantation due to manipulation

Conclusions

A method is described for treating carcinomatous obstruction of the colon and rectosigmoid At the initial operation to relieve obstruction, the colostomy is placed as close to the growth as possible so that both may be resected together at a second and final operation

The advantages include a reduction from three to two in the number of operative stages and therefore reduced risk of morbidity , shorter stay in hospital , and greater freedom of manœuvre, permitting wider excision of the area of lymphatic spread

REFERENCE

Cole, W H (1952) *Arch. Surg , Chicago*, 65, 204

PAROXYSMAL NOCTURNAL HÆMOGLOBINURIA

MARCHIAFAVA—MICHELI SYNDROME

DAVID DOUGLAS
M.D Glasg , F R F P S
CONSULTANT PHYSICIAN AND PHYSICIAN TO OUTPATIENTS, ROYAL INFIRMARY, GLASGOW

JAS C EATON
B Sc , M.B Glasg , F R.I C
CONSULTANT BIOCHEMIST AND LECTURER IN PATHOLOGICAL BIOCHEMISTRY IN THE UNIVERSITY OF GLASGOW

CHRONIC hæmolytic anæmia with paroxysmal nocturnal hæmoglobinuria (P N H) is fairly rare Crosby (195 remarks that 162 cases have been reported since Marchiafava's first description in 1928, but probably the true incidence is much greater The ætiology is unknown The present concept is of a cell defect shared by erythrocytes, leucocytes, and platelets This defect of unknown nature but possibly one of cell stroma protein, renders the erythrocyte abnormally susceptible to a hæmolytic system present in normal plasma

It has been claimed that electron microscopy in some cases has shown abnormal structure in the envelope of the hæmolysed red cell (Matthes et al 1951) Electron microscopy in the case presented below did not support this contention

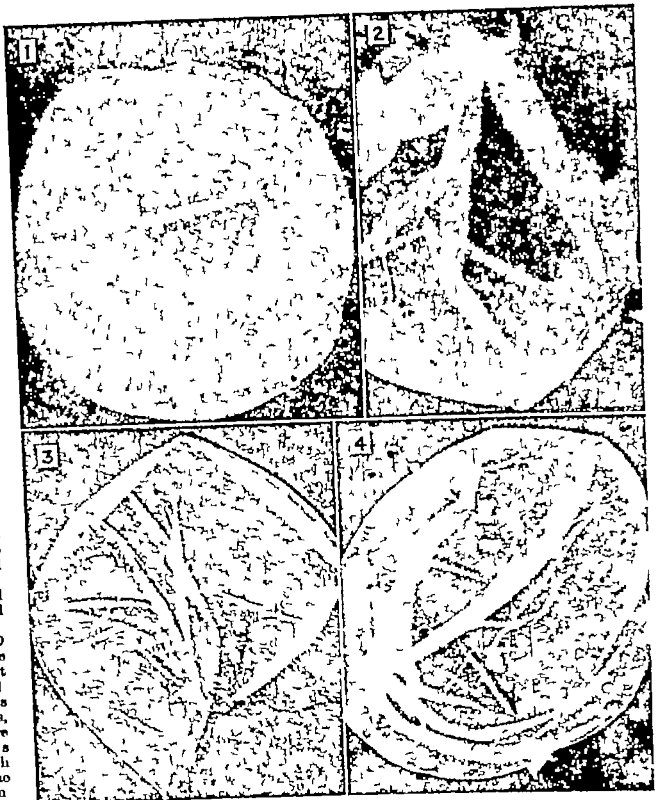
Case-report

A married woman, aged 35, with one child aged 11 years and no history of any previous illness of consequence, she noticed hæmoglobinuria in 1943 while she was pregnant She had it on only one occasion, but she was found, during the puerperium, to have a mild anæmia which did not respond to iron therapy She remained in her usual health thereafter until August, 1953, when she was admitted to hospital as a contact carrier of *Salmonella typhimurium* She was given a course of oxytetracycline, after which her stools were negative r pathogens. She was again found o have an anæmia not responding o iron. Shortly afterwards hæmoglobinuria recurred being present n the first morning specimen of urine but not at other times of the day Her doctor detected slight jaundice which remained, with some fluctuation until readmission to hospital in December 1953 The patient felt tired and weak and had spells of dizziness in the morning lasting about an hour She knew by a feeling of general malaise when she would pass bloodstained urine. There was no history of anæmia or jaundice in her family or of exposure to hæmolytic drugs

The patient was a small and slimly built young woman who was pale and had a lemon yellow tint and a few soft and slightly enlarged glands on either side of the neck but not elsewhere No enlargement of liver or spleen was detected No abnormality was found in the cardiovascular respiratory nervous or alimentary systems. The morning urine was the colour of port wine and contained albumin but no bile

Laboratory Investigations —Examination of the blood showed Hb 9·8 g per 100 ml red cells 3,030 000 per c.mm., and white cells 5400 per c.mm A red-cell fragility test showed that hæmolysis began in 0·5% solution and was complete in 0 35% (control 0 45% and 0·4% respectively) The blood group was A Rh D positive The probable genotype was R2 r (c̄DE c̄de) The direct Coombs test was negative; and when the patient s serum was tested against a large panel of cells, no irregular antibodies were detected Ham s test and Crosby s modification of Ham s test both showed strong hæmolysis of the patient s cells by homologous serum whereas there was no hæmolysis in the control tests. In addition the patient s cells were incubated with an anti A serum which contained a weak anti A hæmolysin; the control cells showed slight hæmolysis, whereas the patient s cells were considerably hæmolysed The Wassermann and Donath Landsteiner tests were negative Between periods of hæmoglobinuria the serum contained small amounts of oxyhæmoglobin and considerable amounts of methæmalbumin Shortly after the passing of dark urine it contained a large amount of oxyhæmoglobin and a small amount of methæmalbumin. The methæmalbumin was never demonstrable spectroscopically and was only detected by plotting absorption curves on a spectrophotometer Electrophoresis of the serum did not reveal any abnormality; likewise electrophoresis of the hæmoglobin within the cells revealed no difference in mobility from that of control samples The dark samples of urine contained variable amounts of methæmoglobin and oxyhæmoglobin. When the urine was freshly passed the amount of methæmoglobin was usually considerable but on standing it disappeared rapidly increasing alkalinity converting it to oxyhæmoglobin. The deposit revealed a few hyaline casts numerous squamous epithelial cells (a small proportion of which contained iron granules within the cells) and very numerous amorphous particles of iron-containing material. No red blood-cells were seen. The urinary excretion of urobilinogen was 3 mg daily The fæces were of normal colour The fæcal excretion of urobilinogen was 238 mg daily

Progress —Hæmoglobinuria ceased spontaneously after five weeks. It has not so far recurred but there has been no improvement in the anæmia. The patient s general condition remains moderately satisfactory There have been no thrombotic or infective complications For these reasons it has not been deemed advisable to give a transfusion of washed cells or anticoagulant drugs which may have a temporary ameliorating effect on hæmolysis



Appearance of normal and P N H erythrocyte ghosts on electron microscopy: 1 normal erythrocyte unshadowed (× 8000); 2, P N H erythrocyte unshadowed (× 12,000); 3 normal erythrocyte shadowed with Au and Pd (× 8000); 4 P.N H. erythrocyte shadowed with Au and Pd (× 8000)

Electron Microscopy —The patient s red cells were examined by electron microscopy and some of the results are shown in comparison with those of normal cells in the accompanying figure The cells, obtained from samples prepared as shown below were separated from plasma or from serum by spinning and hæmolysed with 5 10 or 30 volumes of water The envelopes were separated by centrifuging and were treated with 1% osmium tetroxide for 30 minutes The material was again spun, washed resuspended to a suitable concentration and sprayed on to a supporting film for microscopy Some films were shadowed with gold and palladium at 15 C The following preparations were examined thus: (1) citrated blood; (2) cells from blood allowed to clot spontaneously; (3) cells from blood defibrinated by shaking with glass beads (4) cells from blood defibrinated by stirring with a glass rod; (5) as (3) but after allowing the blood to stand for some days before defibrinating; and (6) as (4) but allowing the blood to stand for some days. Samples 4 5, and 6 were unshadowed None of the photographs showed any significant differences between normal and P.N.H cells. There was no evidence of the spotty or "mesh like" appearance described by Matthes et al (1951)

Discussion

The lytic mechanism in P N H has been studied by many workers, notably Crosby (1953) and Crosby and Bell (1951), the current views and the literature being well reviewed by Crosby (1953) It has been shown that both lytic and inhibitory factors are present in normal plasma, but that the abnormality in P N H does not lie in these factors If P N H cells are placed in normal plasma they tend to undergo lysis, this process being hastened by acidification, normal erythrocytes are not lysed by P N H plasma This explains why transfusion of a P N H patient with normal blood tends to produce a lytic crisis The system present in the normal transfused plasma attacks the abnormal cells of the patient If washed cells only are given, the normal plasma system being absent, no lysis results

Despite much examination no satisfactory explanation is forthcoming for the widely observed tendency of P N H patients to get lysis during sleep It has been repeatedly suggested that diminished excretion of respiratory carbon dioxide during sleep reduces the plasma pH (T H Ham 1939, G C Ham and Horack 1941, Matthes et al 1951), but the evidence for this is not entirely conclusive (Peterson 1949, Crosby and Bell 1951) From in-vitro experiments Peterson (1949) suggested that carbon dioxide has some specific effect not shared by other acids, but Crosby and Bell (1951) and Ham (1939) could not confirm this It appears clear that the lytic tendency is associated with sleep as such and not with posture or time of day Increase of pulmonary ventilation in a respirator during sleep will prevent lysis (Ham 1939, Ham and Horack 1941)

Paroxysmal nocturnal hæmoglobinuria does not appear to be hereditary, only one of a pair of uniovular twins had the abnormality (Crosby 1953) The onset is usually in adult life, the sexes are equally affected It has been suggested that the disease is due to some unknown sensitisation Experiment has failed to reveal any abnormality in the hæmoglobin (McIlvaine and Beard 1951 and our own results) The apparently normal condition of plasma and hæmoglobin in this disease points to the red-cell envelope as the seat of the abnormality Despite the claim by Matthes et al (1951) to have demonstrated lacunæ and a mesh like appearance in electron microphotographs of P N H cells, our findings showed no significant difference between P N H and normal cells Sundharagiati and Wright (1953) found changes similar to those described by Matthes et al in a variety of blood dyscrasias and believe that these were due to artefacts

Splenectomy has been found to be useless or even harmful Treatment with alkali is ineffective (Buell and Mettier 1940), and numerous hormones and drugs have been tried without success by other workers Crosby (1953) showed that dicoumarin may help Thrombin destroys the normal heat stable inhibitor of lysis By preventing conversion of prothrombin to thrombin dicoumarin inhibits this destruction In emergency, transfusion with homologous cells washed free from plasma is effective

Summary

A case of paroxysmal nocturnal hæmoglobinuria is described

The laboratory findings were characteristic Some hæmolysis was present even when there was clinical remission Electrophoretic examination of the hæmoglobin revealed no abnormality Electron microscopy of the lysed red blood-cells showed no difference between their envelopes and those of normal erythrocytes

We wish to thank Miss H. M Laird, of the Beatson Memorial Hospital, for preparing and reporting on the electron microphotographs, Dr J Wallace, of the West of Scotland Blood Transfusion Service, for serological examination of the blood, and Dr David Smith, of Glasgow Royal Infirmary, for permission to examine the patient

REFERENCES

Buell A. Mettier, S R. (1940) *J Lab clin Med* 26, 1434
Crosby, W H (1953) *Blood*, 8, 769
— Bell, J C (1951) *Rev Hémat* 6, 299
Ham, G C, Horack, H M (1941) *Arch intern Med* 67, 735
Ham, T H (1939) *Ibid*, 64, 1271
McIlvanie, S K, Beard, M F (1951) *Blood*, 6, 936
Marchiafava, E (1928) *Policlinico, sez med* 35, 109
Matthes V M, Schubothe, H, Lindemann, B (1951) *Acta hæmat* 5, 193
Peterson, A (1949) *Dtsch Arch klin Med* 196, 486
Sundharagiati, B, Wright C S (1953) *J clin Invest* 32 979

ON THE SEX OF CANCER AND TERATOMATA CELLS

AMÂNDIO S TAVARES
M B Oporto
ASSISTANT, DEPARTMENTS OF GENERAL AND ANATOMICAL PATHOLOGY, FACULTY OF MEDICINE, OPORTO UNIVERSITY, PORTUGAL

A MORPHOLOGICAL sexual difference in the nuclei of nerve-cells of cats was found by Barr and Bertram (1949, 1951), and later work showed that a chromatin mass called "sexual chromatin" or "corpuscle of Barr" is seen in about 75% of nuclei of various tissues in females, but is seldom detected in males (Barr et al 1950, Graham and Barr 1952)

These findings have been applied to the diagnosis of sex in other animals and in man (Moore and Barr 1954). For instance, nuclear sex has been studied by this method in transvestites (Barr and Hobbs 1954), hermaphrodites (Moore et al 1953, Barr 1954), and Turner's syndrome (Polani et al 1954) Using a slightly modified technique, Emery and McMillan (1954) say that, except for some doubtful results obtained in necropsy material in the newborn, the method is reliable when applied to children

Hunter and Lennox (1954), who examined spino-cellular epitheliomata of the skin, conclude that cancer cells are of the same sex as the patient, but, as regards teratomata, 5 out of 9 in males were heterosexual whereas 12 teratomata in women were all of the same sex as the patient If this latter finding is applicable generally, we will have to revise our ideas of the genesis of teratomata

Meanwhile we add to the findings of Hunter and Lennox (1954) and of Cruickshank (1955) our findings in 34 teratomata and 110 cancers

Method

We used formalin fixed paraffin embedded sections 5–8 μ thick stained with hæmatoxylin and eosin, and

TABLE I—SEX OF CANCER CELLS

Tumour	Sex of patient					
	Male			Female		
	Average (%) no of cases		Range (%)	Average (%) no of cases		Range (%)
Carcinoma of skin	5 9	24	1 5–17 0	72 9	27	[illegible]
Undifferentiated carcinoma of skin		2	1 0– 4 0		3	[illegible]
Primary carcinoma of liver		1	11 5		3	[illegible]
Adenocarcinoma of stomach	5 6	5	2 5– 9 5	69 8	5	[illegible]
Papillary carcinoma of bladder	6 4	5	3 0–12 0	70 2	5	[illegible]
Adenocarcinoma of ovary				73 3	5	[illegible]
Seminoma of testis	4 0	5	3 0– 5 5			
Carcinoma of kidney	7 5	5	4 0–11 0	71 9	5	[illegible]
Myosarcoma	8 6	8	5 5–15 0		2	[illegible]

TABLE II—SEX OF TERATOMA CELLS

Sex of patient	Sex of teratoma cells: Male: Hunter and Lennox (1954)	Male: Cruickshank (1955)	Male: Present investigation	Male: Total	Female: Hunter and Lennox (1954)	Female: Cruickshank (1955)	Female: Present investigation	Female: Total
F					12	2	25	39
M	4	2	5	11	5	1	4	10
Total	4	2	5	11	17	3	29	19

χ^2 (for 1 : 2 ratio) = 1·999 P = 0·106
χ^2 (for 1 : 1 ratio) = 0·0476 P = 0·962

controls were stained by the Feulgen method. We found fixation to be of greater importance than the method of staining.

Counts were made of nuclei containing the sexual chromatin, as defined by Barr and his colleagues, and percentages were established for at least 200 cells. Doubtful nuclei were counted as half positive, half negative. Immature and degenerated cells were excluded and only one nucleus was examined in the multinucleated elements so commonly found in cancer.

This method gave statistically significant results ($P = 1 \times 10^{-11}$) with a relatively small standard deviation (s = 2·5), in the case of normal skin cells of 40 adults, the sexes being well separated (females 60–80%, males 1–18%) and the two frequency curves showing diverging skewness.

Results

Cancer

In 110 sundry malignant tumours, taken at random for each variety from the cases registered in the department of anatomical pathology in the University of Oporto, the sex of the patient and that of the tumour were the same (table I). The range of results shows no significant difference between normal and cancer cells, and identical percentages were obtained when both were examined in the same section. Neither localisation nor type of neoplasm influenced its 'sex'; the only exceptions were two undifferentiated carcinomata of the skin in women; the low figures (27% and 55·5%) may be explained by the immaturity of the nuclei in these neoplasms.

The number of chromatin-containing cancer cells and mature histiocytes in the stroma of the tumour were counted in 20 cases and differed very little (t = 0·632, d.f. = 10). The histiocytes proved much more reliable than epithelium, because in the undifferentiated carcinomata mentioned above the histiocyte-counts were 70·0% and 74·5%.

Teratomata

Our findings in 34 teratomata (25 from women and 9 from men) were very similar to those of Hunter and Lennox (1954): all 25 from women were 'feminine', whereas 4 of the 9 from men were 'masculine'. If we combine our findings with those of Hunter and Lennox (1954) and Cruickshank (1955) we find that 48% of teratomata in males are hetero-sexual. This fact argues against two current theories of the genesis of teratomata: the blastomere theory and that of parthenogenetic division of a diploid cell. On the other hand, not much support is lent to the theory of gamete (or at least haploid cell) conjugation proposed by Hunter and Lennox (1954), which calls for a ratio of 1 XX : 2 XY : 1 YY teratomata. According to Moore and Barr (1954) only the pair of XX chromosomes determine the appearance of sexual chromatin. This reduces the genetic ratio to 1 XX : 3 (XY + YY) or, if YY cells do not survive (and we know very little on this subject), to 1 XX : 2 XY. The χ^2 test of departure gives a probability rather close to the statistical level of significance (table II).

The objection that teratomatous material, since it is often either undifferentiated or immature, is unsuitable for this study does not hold, at least for our series: only nuclei from mature epithelial, connective, and nervous tissue were counted. On the other hand, if lack of cell differentiation (which may only cause a depression in percentages, as we have shown) influenced our results, these would be reversed and heterosexuality would be found in women alone.

A far greater number of teratomata will have to be studied before any theory emerges from these findings. However, one explanation of a 1 : 1 ratio is, perhaps, the parthenogenetic division of haploid cells followed by chromosome reduplication, forming 100% of XX cells in the female, and 50% of XX and 50% of YY cells in the male. Of course this means attributing a pair of YY chromosomes to the cells of some teratomata, and we do not know anything about their viability.

REFERENCES

Barr, M. L. (1954) *Surg. Gynec. Obstet.* 99, 184.
— Bertram, E. G. (1949) *Nature, Lond.* 163, 676.
— — (1951) *J. Anat.* 85, 171.
— Bertram, L. F., Lindsay, H. A. (1950) *Anat. Rec.* 107, 283.
— Hobbs, G. E. (1954) *Lancet*, i, 1109.
Cruickshank, D. B. (1955) *Ibid*, i, 253.
Emery, J. L., McMillan, M. (1954) *J. Path. Bact.* 68, 17.
Graham, M. A., Barr, M. L. (1952) *Anat. Rec.* 112, 709.
Hunter, W. F., Lennox, B. (1954) *Lancet*, ii, 633.
Moore, K. L., Barr, M. L. (1954) *Acta anat.* 21, 197.
— Graham, M. A., Barr, M. L. (1953) *Surg. Gynec. Obstet.* 96, 641.
Poland, I. L., Hunter, W. F., Lennox, B. (1954) *Lancet*, ii, 190.

LOCAL TRANSMETATARSAL AMPUTATION IN ARTERIAL INSUFFICIENCY OF THE LOWER LIMB

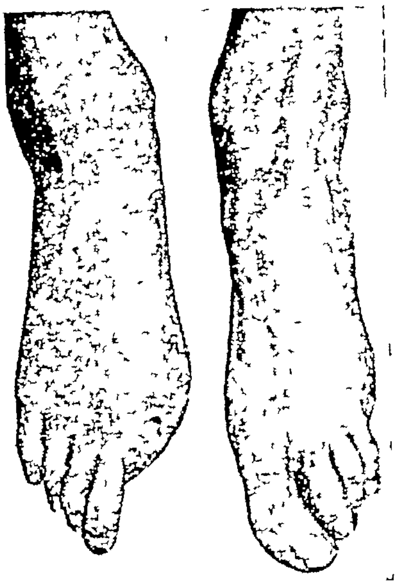
A. G. NORMAN
M.A., M.B. Camb., F.R.C.S.
SENIOR SURGICAL REGISTRAR, ST. THOMAS'S HOSPITAL, LONDON

ARTERIAL insufficiency of the lower limb is nowadays treated more conservatively than formerly, preserving as much of the limb as is compatible with healing and sound function. In gangrene of the foot amputation at the metatarso-phalangeal joint commonly proves unsatisfactory, and in the past these unsuccessful cases were treated by high amputation. We now attempt to save more limbs by local transmetatarsal (ray) amputation.

In the present series of 12 cases involving 14 limbs with gangrene of toes, only one of the five toes was involved in 10 limbs. This suggests that there must be some local fault in the circulation of the affected toe. Our arteriographic studies have led us to believe that gangrene in the arteriosclerotic patient results from multiple blocks, and we suspect that in these cases the final block is in the plantar *metatarsal* arteries as they pass the head of the metatarsal bones (Rob 1954). Although the toes, unlike the fingers, have *both* dorsal and plantar digital arteries, it is the plantar arteries that carry most of the blood supply.

In local transmetatarsal amputation the toe and the head of the corresponding metatarsal bone are removed through an anterior racket incision. The aim is to amputate above the level of the arterial block. Great care must be taken to clear away all splinters of bone, since these, if unremoved, delay healing.

Of the 12 patients (9 men, 3 women), whose average age was 61·5, all had diffuse arterial disease and 5 were diabetic. The main manifestations in the 14 affected limbs were: *dry gangrene* (6 cases), *ulceration* (5), and



Foot after local transmetatarsal amputation of right first toe and left fifth toe

cold blue toe (3), and the average length of history was four months In 5 cases these manifestations had been preceded by claudication in the calf

The digits most commonly affected were the first, fourth, and fifth The numbers affected in the 14 limbs were first digit, 4, second digit, 1, third digit, 1, fourth digit, 7, and fifth digit, 5

The results at three to fifteen months after operation were as follows healed, 7 (primary healing 5, delayed healing 2), unhealed, 2, required high amputation, 5 Thus the failure rate was 36%, which is similar to the 37% in a series of total transmetatarsal amputations described by Warren et al (1952)

Analysis does not reveal any sign by which failure can be predicted Failure was unrelated to age, sex, or the presence of diabetes

This operation is designed to remove as little as possible of the gangrenous limb McKittrick (1946), McKittrick and Risley (1949), Furste and Herrmann (1948), and others have attempted to achieve this end by total transmetatarsal amputation, thereafter the foot functions well (unlike the state after amputations at the tarsus by the method of Lisfranc and Chopart), and their results are similar to those described here

After local transmetatarsal amputation the healed foot (see figure) is functionally satisfactory, and the limited follow up in the series described here shows that the wound remains satisfactorily healed In 1 of the diabetic patients a perforating ulcer of the foot developed, but the amputation site remained healed

I am indebted to Prof George Perkins for introducing me to this operation, to Mr F B Cockett for criticism and advice, to the physicians and surgeons of St Thomas's Hospital for permission to describe their cases, and to Mr K G Moreman for the photograph.

REFERENCES

Furste, W, Herrmann, L G (1948) *Arch Surg, Chicago*, 57, 15
McKittrick, L S (1946) *New Engl J Med* 235, 929
— Risley T S (1949) *Ann Surg* 130 826
Rob G C (1954) *In* Recent Advances in Surgery Edited by H. C. Edwards London p 329
Warren, R, Crawford, E S, Hardy, I B jun McKittrick, J B (1952) *Surgery* 31, 132

Medical Societies

ASSOCIATION OF CLINICAL PATHOLOGISTS

THE 54th meeting of this association was held in Douglas, Isle of Man, on April 13–15 We publish summaries of some of the papers presented at the meeting

Typing in Epidemiological Investigations

Dr W H BRADLEY said that Griffith had first introduced serological typing of hæmolytic streptococci in 1926, and by 1934 a range of 27 reference types was available Craigie and Felix had shown in 1938 that bacteriophage typing of *Sal monella typhi* was practicable, and by 1947 they had prepared a couple of dozen reference phages The significant fall in the mortality of streptococcal disease (particularly puerperal sepsis) between 1934 and the advent of sulphonamides probably reflected the increase in the possibility of outbreak control stimulated by the Griffith's typing

The mortality of enteric fever in the United Kingdom had fallen away more rapidly than in other European countries, and this improvement coincided with the introduction of phage-typing Dr Bradley thought that because typing made epidemiological investigations more convincing and more fun their quality was improved and preventive medicine became more effective Moreover, epidemiological and ætiological concepts had been reshaped The rôle of type 12 and to a lesser extent type 4 streptococci in nephritis was an example It was now realised that the many distinct serological or phage types within a species were acting independently and that their specificity was enduring

Antigenicity of Toxoids and Sympathomimetic Drugs

Dr J UNGAR described how water insoluble mineral carriers such as aluminium or calcium salts, tapioca, oils and fats, and, recently, bacterial suspensions, had been used to increase the efficiency of prophylactic toxoids and thereby reduce the number of injections required Their presence caused local irritation, which was most severe with aluminium and calcium salts and least severe with bacterial suspensions, he had used *Hæmophilus pertussis* vaccines successfully in the past

As the use of vaccines might be undesirable in hypersensitive persons, Dr Ungar had tried to improve the antigenic efficiency of diphtheria toxoid by altering the rate of absorption with drugs exerting a local tissue effect Adrenaline hydrochloride (1 in 1000 to 1 in 2000), benzedrine hydrochloride (1 in 250), ephedrine hydrochloride (1 in 250), and histamine (0 5 μg per ml) had been used Two amines, β phenylethylamine and phenylethylamine acetate, which have no vasoconstrictor action, were included as controls When tested in guineapigs the sympathomimetic vasoconstrictors greatly enhanced the response to diphtheria toxoid Combination with histamine caused only slight enhancement and the two control amines did not affect the response to the toxoid Vasoconstrictors might prove useful for enhancing the efficiency of diphtheria toxoid, especially when children hypersensitive to injections of antigen were being immunised

Lung Carcinoma in Hæmatite Miners

Dr J STEVEN FAULDS said that the incidence of primary cancer of the lung in iron ore miners in Cumberland over the last twenty three years was 9 4%—four times that found in a control group of males of similar age and habits, but different occupation. The site of the tumours corresponded to the areas where the characteristic massive fibrosis developed, and the primary lesion was not in the main bronchus, but in a peripheral lung field The observed association of squamous celled lining to a chronic abscess cavity and a squamous carcinoma in the same area suggested that the tumour arose in the sidero silicotic mass Since silicosis was a frequent finding in other kinds of mining and an association between silicosis and bronchial cancer was not common, it was difficult to give a reason for the increased frequency of carcinoma found in iron ore miners

Lower-nephron Nephrosis

Dr S SEVITT showed that distal tubular necrosis (lower nephron nephrosis) in the kidneys of burned patients was commoner among those who had an adequate or normal flow of urine than in those with severe oliguria or anuria Clinically and biochemically there were uræmic and non uræmic forms with little or no oliguria The uræmic group was important to diagnose because the recent advances in therapy may reduce its high fatality Morphologically these kidneys showed a *diffuse* distal tubular necrosis in which hæmoglobin casts were prominent Many nephrons were involved and although the morphology was no different from that found in those with anuria or severe oliguria, tubular function was impaired

The finding of non-oliguric uræmia in an injured man with histological distal tubular necrosis of the kidneys indicated that the phenomenon was not restricted to burned subjects In the non uræmic condition there was no significant azotæmia during the illness, and death was due to non renal complications. Histologically the kidneys of these patients should show either a *focal* type of distal tubular necrosis, associated with few casts and affecting only a minority of the nephrons, or the healing or healed evidence of a recent focal attack.

Blood-ammonia Levels in Liver Disease

Mr A G Riddell described experiments on dogs with portacaval anastomoses which had shown that a neurological disorder can be produced in these animals by intoxication with ammonia Histological examination of the brains of these dogs showed the same change in the protoplasmic astrocytes as in patients dying in hepatic coma In hepatic coma a raised blood ammonia level was found The type of hepatic coma that followed bleeding from œsophageal varices was analogous to the syndrome seen in dogs and the ammonia was derived from the blood in the alimentary tract While blood ammonia determinations were required in the diagnosis and management of unusual cases, they were not required in the routine treatment of hepatic coma.

Fibrinous Vasculosis

Dr A. C Lendrum suggested this term for the deposition in blood vessel walls of a material giving the staining reactions of fibrin. The commonest cause of this was severe stagnant ischæmia, as in infarction or torsion Other causes were drug-induced hyperergic arteritis extreme hypertension, polyarteritis nodosa and occasionally acute rheumatic disease disseminated lupus erythematosus and dermatomyositis The fibrin was commonly seen under an intact endothelium sometimes as a complete ring round the intima From this level it either seeped into the wall (vessels of infarcted zone) or was injected across the media (in extreme hypertension) to spread out along the external elastica through which it may erupt focally At sites where a layer was traversed, there was in all types of fibrinous vasculosis a stretching and distortion of the nuclei as if they had been subjected to mechanical extension. Gross cellular aggregation was seen in and around a few some or all of the affected vessels. Intravascular thrombosis was uncommon except in small vessels, even when the vessel wall was a mass of fibrin

The most extreme degree of fibrinous vasculosis had been seen in the pulmonary vessels in 2 cases of mitral stenosis; and the next degree in infarcted organs. The three forms of fibrinous vasculosis, the stagnant hypertensive and hyperergic, appeared to be histologically indistinguishable All might be regarded as a form of exudation due to an upset between the pressure in the vessel and the permeability of the lining

Hæmophilia and Christmas Disease

Dr Rosemary Biggs discussing the diagnosis of these ditions said that the laboratory tests of clotting function t have been used were the whole blood clotting time the thrombin-consumption test and the thromboplastin eration test. In hæmophilia the clotting time was pro ged in more than half of the patients, but patients who quite severely affected may have a normal clotting time ilarly the prothrombin-consumption test usually gave ormal results in hæmophilia, but with some samples ults were normal The thromboplastin generation test e more reliable results in hæmophilia blood than either the other tests, and using this technique it was possible to tinguish patients with hæmophilia from those with Christ s disease About 10% of patients previously diagnosed having hæmophilia were found to have Christmas disease the patients with Christmas disease many were rather htly affected with a normal clotting time and consumption prothrombin

Interstitial Emphysema in the Newborn

Dr John L Emery in a consecutive series of 100 infants ing within seven days of birth had found that 7 out of f- ll term children had died with interstitial emphysema ter congenital deformities it was the commonest single cause of death The condition was spontaneous and not due to artificial respiration it was probably caused by the expulsive efforts of crying in lusty infants who had inhaled vernix or mucus.

OPHTHALMOLOGICAL SOCIETY OF THE UNITED KINGDOM

Diamox in the Treatment of Glaucoma

The 75th congress of the Ophthalmological Society of the United Kingdom, held in London on April 28–30 included a symposium on 'Diamox' in the Treatment of Glaucoma Diamox (2-acetylamino 1 3 4 thiadiazole 5 sulphonamide) has been known for some years to have a powerful inhibitory effect on the enzyme carbonic anhydrase and it has been used in the treatment of congestive heart-failure because of its diuretic effect[1]

Mr E S Perkins analysed the results in 58 cases treated at Moorfields Eye Hospital, and confirmed the value of this drug in controlling all of the major categories of glaucoma in about 50% of all cases—congestive glaucoma, simple glaucoma and glaucoma secondary to iritis and to trauma—the tension was brought well under control while of the remaining cases about half were controlled partially or for a short period This effect was potentiated by the simultaneous use of miotics The dosage suggested was 500 mg initially followed by 250 mg six hourly after a few days this dose could generally be reduced to twice or thrice daily at which level it should be maintained Side-effects were rarely disturbing diuresis and paræsthesiæ were usually very transient Mr Perkins concluded that the particular value of diamox was in the control of acute congestive glaucomatous crises where it allowed the eye to quieten for a subsequent drainage operation; in certain cases of simple glaucoma where miotics had failed to achieve effective control, and in cases of iritis glaucoma in which the tension could be controlled until the initiating iritis had been allayed

Dr John Gloster described his estimation of the effect of diamox on the intra-ocular pressure of normal rabbit eyes. He found that an intravenous injection of diamox caused a drop in the intra-ocular pressure within one minute the speed of this action suggested that it was due to a direct effect on the secretion of aqueous humour in the ciliary body The changes estimated by the insertion of a cannula into the aqueous, were significant only with doses larger than those used clinically

Dr Maurice Langham reported the results of further experiments on rabbit eyes Observations were made first on the effect of diamox on the distribution of bicarbonate between the aqueous humour and the plasma, since it might be assumed that the inhibition of the production of hydroxyl ions would decrease the osmotic pressure of the aqueous and thereby reduce its formation The influence of the drug was assessed according to the permeability of the blood aqueous barrier and the flow of the aqueous humour by measuring the rate of accumulation of fluorescein in the aqueous humour after intravenous administration It was found that, although the bicarbonate in the aqueous diminished after the administration of diamox its concentration relative to that in the plasma was unchanged The method by which diamox reduced the formation of the aqueous thus remained uncertain; the results of his experiments did not show whether diamox in fact exerted its effect by its systemic action or through a non specific inhibition of aqueous secretion

Prof G P Sourdille (Nantes) reported clinical observations which agreed essentially with those described by Mr Perkins

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[1] See *Lancet* April 2 1955 p 706

Reviews of Books

Practical Obstetric Problems

IAN DONALD, M B E, M D Lond, M R.C O G, regius professor of midwifery, University of Glasgow London Lloyd-Luke 1955 Pp 578 45s

IN many ways this is an admirable book, but it is not addressed consistently to any particular group of readers, and one cannot easily say just what kind of book it is. The title and part of Professor Donald's preface suggest that it is largely a reference work for the practising obstetrician, but, though the practising obstetrician will find much profit and enjoyment in its discussion of controversial problems, it leaves out things one would expect it to contain It is not a textbook, for the anatomical and physiological ground-work of obstetrics has been deliberately omitted Perhaps it will be of most value to those who have a little experience of obstetrics and are sitting a higher examination —though these will have no need of the details of simple obstetrical procedures (such as toilet of the vulva before forceps delivery) nor of some of the discussions of matters that belong to undergraduate rather than postgraduate teaching

The points at which fellow experts will take issue with the author mostly concern manipulative obstetrics In the section on manual correction of the fœtal head in the occipito posterior position, a good method is described for altering the fœtal position, but no reference is made to the alternative techniques, such as rotating the shoulders by the internal hand or correcting the malposition by placing the hand over the fœtal face In the section on breech delivery the description of the rotation of the anterior shoulder posteriorly does not mention the desirability of over correction if the back of the fœtal head is to remain directed to the symphysis The statement that "the lateral position for forceps delivery has been abandoned" takes no account of those who are convinced that the lateral position confers at least the two advantages of a reduced risk of anæsthesia and less perineal damage Some, too, will disagree with the opinion (on twins) that "if a general anæsthetic has been necessary in the course of delivery of the first child it is usually preferable to discontinue it while awaiting the arrival of the second." Sweeping statements such as "Cæsarean myomectomy is an indefensible operation" and "undoubtedly" routine X ray pelvimetry in all primigravidæ "will come in time" belong perhaps to the cut and thrust of debate rather than to the printed page

Against these objections must be set the important fact that the book conveys much of the author's zest Some of its parts, and some of its sentences, are too long, but it is often very readable Many will be grateful for its robust, uncompromising approach, and above all for its stimulating enthusiasm

Memoirs of My Nervous Illness

DANIEL PAUL SCHREBER Translators and editors IDA MACALPINE, M.D, RICHARD A HUNTER, M.D, M.R C.P, D.P M London Wm Dawson 1955 Pp 416 £1 15s

AUTOBIOGRAPHICAL accounts of mental illness are valuable documents, especially when written by patients of high intelligence, gifted with powers of self-observation and accurate recollection These qualities were undoubtedly possessed by Daniel Schreber, a judge of the supreme court in Saxony, who developed a severe schizophrenic illness in late middle life His account of his experiences in this illness, first published in 1903, was the subject of a study by Freud eight years later Freud's paper has become important in the development of psycho-analytic theory about psychoses, and the Schreber memoirs are often mentioned, but usually by people who have not read them, because the book has become scarce and has never been translated from German Dr Macalpine and Dr Hunter have now made good this deficiency

Their translation does not always run smoothly, but it may well be a faithful reproduction of Dr Schreber's style Schizophrenics do not write with terse and graceful precision, nor perhaps do judges, and the reader is willing to accept the translators' disconsolate reference to Schreber's cumbersome and involved language They give examples of his neologisms in an appendix They have fallen into a few well known traps—such as translating *Moment* as "moment" instead of "factor"—but these are trifling blemishes in a large undertaking Besides the *memoirs*, the book contains a clinical and historical introduction by Dr Macalpine and Dr Hunter, a reprint of their informative psychopathological article on the Schreber material, and translations of the psychiatric reports on Schreber, the legal statement in which he asked to be given back control over his affairs, and the judgment of the court which heard this appeal.

The translators ride a few hobby-horses, as their incidental polemic against physical forms of treatment shows, but the grateful reader will not begrudge them this by-product of their labours for his benefit, he may even, unless an orthodox psycho-analyst, find their irreverent re-examination of some central issues of Freudian psychopathology stimulating

Examen clinique et traitement d'un endocrinien

A. LICHTWITZ and R PARLIER, Hôpital Lariboisière Paris Paris L'Expansion scientifique française 1954 Vol I Pp 456 Fr 5200 Vol II Pp 392 Fr 4800

To apply recent advances in endocrinology demands some understanding of the experimental techniques which produced them Doctors are often ill equipped by their training to follow the methods of diagnosis and treatment that have evolved Dr Lichtwitz and Dr Parlier, in this frankly didactic account of endocrinology in its modern setting, have, by their attention to layout, tables, and diagrams, done much to explain the scientist's findings to the clinician In the preface they write "We hope the jealous guardians of pure biological science will pardon certain abuses of simplification, remembering that our aim is to reach not only those doctors who wish to perfect their knowledge of modern endocrinology, but all those who are harassed by the problems of general pathology" But the questioning and thoughtful reader may be disappointed

Dr Lichtwitz and Dr Parlier deal first with some general principles and then with the hypophysis, the thyroid, the ovary, and, in the second volume, with the testes and the suprarenal Throughout, the influence of Selye makes itself strongly felt The book is a useful guide to the French literature and in particular to the authors many original articles. It is lavishly produced, and misprints are mostly in the references but the index is unfortunately sketchy

The Challenge of Man's Future

HARRISON BROWN London Secker & Warburg 1954 Pp 290 21s

Prof Harrison Brown is a chemist with an expert's knowledge of the earth's material resources, an American's optimism about human capacity, and a citizen of the world's awareness of the rake's progress and the fateful hour Like Sir Charles Darwin he sees the ultimate consequence of an uncontrolled growth of population and a spendthrift use of our resources, but he is not convinced that there is no escape from this doom

He foresees three possible patterns of life reversion to the agrarian existence of the pre-industrial period a completely controlled, collectivised industrial society in which war has been abolished, new energy sources are utilised, and population is kept stable, a world wide free industrial society, labile but capable of permanence The last, the most desirable and to our favoured Western minds the expected outcome of "progress," is the most difficult to achieve since it requires efforts beyond anything human beings have so far compassed They must adapt themselves to constant change, preserve freedom while accepting control of reproduction, aggression, and other old desires, and use their intelligence and self restraint now in order to conserve their dwindling extra human resources and so turn to most use their inner resources of wisdom and generosity Though this is the conclusion of the matter, and gives only chastening comfort, it follows a well-organised factual account of what is happening and what must later happen if we continue in our present courses the account is objective and the main argument irrefutable

THE LANCET

LONDON SATURDAY, MAY 7, 1955

Research in General Practice

There is a danger inherent in the work of general practice that the very great variety of subjects for practice and thought in a day's work may lead to a superficial and desultory curiosity rather than an eagerness for study

WHEN he offered this reflection in the first John Matheson Shaw lecture[1] of the Royal College of Physicians of Edinburgh last November, Prof JAMES MACKINTOSH was discussing the opportunities for research now opening before general practitioners. A Sassenach might have softened the blow with some reference to the fatigues of the family doctor's day, but Professor MACKINTOSH merely added that "it is easy to spread a thin layer of butter on the bread of idleness." This bracing approach has much to commend it, for some of the past attempts to get general practitioners to contribute to research have started hopefully but died of inanition. Too often self-chosen projects lose their charm for men working in isolation, especially during winter epidemics. Modern research is often done best by a team, and the College of General Practitioners[2] is surely right in encouraging group projects while at the same time offering information and help to the investigator who prefers to work alone.

At the end of 1954, the register of members willing to take part in research maintained by the research committee of the college council, contained some 380 names, sent in from every part of the Commonwealth. Research committees of 22 faculty boards have been formed in the British Isles and overseas composed of members and associates of the college and also coöpted members from local university or medical-school research departments. The college research advisory panel composed of experts in various medical fields, has been strengthened during the year. Scotland has its own research committee of the Scottish council with its own research advisory panel.

Four types of general practitioner research are being forwarded: college-sponsored investigations, studies by groups of doctors, faculty sponsored investigations, nd individual investigations. The college sponsored vestigations deal with subjects which can be studied ly in general practice, or studied there better than hospitals or laboratories.

A measles investigation to assess the value of sulphomides and antibiotics in preventing complications is ready in progress, and has only been handicapped (the port remarks sadly) by the low incidence of measles in 54. Better things are expected of 1955 and a report may published by the end of the year. A national morbidity rvey is being planned in collaboration with the egistrar-General's department; and a college records nit is being set up which should enable morbidity atistics to be recorded in a comparable way throughout e United Kingdom and overseas. Discussions with e Ministry of Health have resulted in the release of ational Health Service records of dead patients to ctors needing them for research purposes. It has en suggested that clinical trials of therapeutic substances might be made by general practitioners, but this introduces some ethical problems to which the college is rightly giving serious thought. Finally the epidemic observation unit of the college has coöperated with the Public Health Laboratory Service in collecting specimens from suspected cases of influenza for identification of the virus. Through this unit one member of the college has already brought to light an outbreak of Q fever in the South West; and specimens from a recent outbreak of infective hepatitis in the South East have been collected and studied.

Among the study-groups, one is engaged in observing the clinical patterns of acute respiratory infections; another, interested in hereditary diseases, is examining the incidence of hypertrophic pyloric stenosis in the children of people who have themselves survived Rammstedt's operation; a third group is investigating the value of tonsillectomy; a fourth interested in psychosomatic disorders, is making a study of asthma and migraine; and a fifth small group is concerned with *asthma in children*.

Faculty-sponsored investigations include one into obstetrical work in South West England; a study of the symmetry of heads of babies in Northern Ireland to determine whether cranial asymmetry is related to right handedness or left-handedness; a study, in Yorkshire, of the course of cancer in patients who for one reason or another have not been treated; and an epidemiological survey in South East England of non-notifiable diseases including glandular fever, infective hepatitis, and epidemic winter vomiting.

These studies have been started with great enthusiasm but the college has it in mind, from the history of earlier collective investigations, that too great a dispersal of effort may lead to disappointment, and moreover (Professor MACKINTOSH notwithstanding) that there is a limit to the amount of voluntary work a family doctor can undertake over and above his practice. They are therefore wisely planning rather to consolidate the research work begun than to expand into new fields during the coming year.

It is interesting to compare this promising beginning with the research programme Professor MACKINTOSH foresees for general practitioners in years to come. The Public Health Laboratory Service, as he points out, has greatly added to their powers to contribute to systematic research; and he hopes that before long a more organised system of diagnostic centres will be developed and take the place of the health centres—"which are now by general consent slipping back into the waters of Lethe." These, like the Nuffield diagnostic centre at Corby,[3] would be staffed by technicians working under the supervision of specialists, and here general practitioners would have direct access to technical help in the more straightforward types of bacteriology, radiology, and pathology—or could, if they wished, undertake laboratory procedures themselves.

First in his list of possible studies Professor MACKINTOSH puts hereditary defects and diseases, for family doctors, and especially old established firms of doctors have a better chance than most of noticing what happens from generation to generation. They can assess the significance of the eccentric relative and the slow child; can turn up records of stillbirths, neonatal deaths, minor congenital abnormalities, hæmophilia, Huntington's chorea, and pyloric stenosis; can observe the effects of common complaints on patients and their environment; and can assess the long-term effects of remedies old and new, and the protective value of vaccines. They alone have the chance of seeing the onset and full course of the diseases associated with old age, and can investigate both the basic and the precipitating causes of the so-called stress diseases They have remarkable opportunities, of which many of them make full use, of gaining skill in prognosis , and many a young doctor joining an old firm is startled out of his scientific calm by the uncanny skill of the senior partner in predicting the immediate and remote outcome of disease As Professor MACKINTOSH says, the true effects of pregnancy on chronic disease are largely unknown at specialist level Again, though the gross pathology of established disease can be seen and learned in hospital, the delicate innuendos of early disorder are to be apprehended only in general practice They are learned by watching the same patients for a lifetime Mental sickness, which sometimes has its origins in human relations, gives the general practitioner another field for study " The observation of years in a mental hospital or psychiatric clinic may not reveal as much about such patients in their true environment as the general practitioner learns in the course of his daily plodding " , and he it is, at present, who undertakes most of the follow-up and aftercare of patients who have been treated in mental hospitals Epidemiology still has many questions to be answered some incubation periods are still uncertain, and the modes of spread of many diseases are far from clear Professor MACKINTOSH notes the work in this field already being undertaken by the college, but mentions other possible inquiries—not only into the well-known infections such as chickenpox, herpes zoster, and poliomyelitis, but into local non-infectious diseases such as goitre and dental caries , and into chronic disorders such as rheumatism and bronchitis Finally, he suggests there is plenty still to study in the field of normal health and physiology—the disturbances of puberty and the menopause, the male climacteric, the onset of presbyopia, the significance of bodily and emotional types, and " the long fascinating story of child development "

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[1] Research in General Practice. Edinburgh: Royal College of Physicians. 1955. Pp. 38.

[2] Second Annual Report 1954. Pp. 160.

[3] *Lancet* 1954, i, 871.

So much for the programme but there are, he hints, obstacles The first is the medical curriculum, which not only fails to prepare the student for research under the conditions of medical practice but introduces him mainly to the late stages of disease, gives him the scantiest notions of the relations of sickness to social and industrial life, and does not equip him with enough elementary statistics to conduct simple investigations in the field of general practice Given an early understanding of statistical methods and of the importance of controls he would quickly recognise how little is other apparatus needed for important work two eyes, a pen, and a record card often suffice Other obstacles are the want of liaison between general practitioners and consultants, the scarcity of leisure, the broken time, the prejudice of patients (" people in general have a respect almost amounting to awe for research, but they do not enjoy being the subjects of investigation themselves "), and the absence of a stimulating atmosphere, such as is found in hospital or laboratory But all these obstacles, he urges, can be overcome The college is already playing its proper part by giving help and guidance (particularly in the matter of collecting accurate statistics), by organising research teams and groups, and by keeping keen people [illegible] with one another and with experts in their subjects . Other incentives must come from elsewhere—from the medical schools, which must equip their students better for research , from the Ministry of Health, which can distribute information about minor disorders (bronchitis, common colds, and the neuroses) which are responsible for much ill health, and as a by-product from group practice which gives the doctor time for reading, writing attending clinical meetings, looking after his own health , and developing more fully his skill in his profession

Cell Type in Bronchial Carcinoma

NO-ONE would suggest that surgery is an adequate weapon in the treatment of bronchial carcinoma, but it is the best we have , and with modern technique roughly one quarter to one third of patients who have " curative " resections survive operation by at least five years[1–6] It is now clear that the prognosis in these cases is greatly influenced by the cell type of the tumour[5–8] Bronchial carcinoma is usually classified histologically as squamous cell, adenocarcinoma, or undifferentiated , but KIRKLIN et al[6] consider that it is worth subdividing the undifferentiated group into small cell carcinoma and large cell carcinoma The cells in small cell carcinoma have little cytoplasm, they are irregularly arranged, and as the nuclei are often spindle shaped the term " oat cell " is commonly applied to this group The cells in KIRKLIN's large-cell type have more cytoplasm, but the other histological features are variable, sometimes resembling those of the small cell variety and sometimes those of the squamous cell type, so that pathologists recognising only three groups would put them in one or other of these categories

The prognosis in the small-cell (oat-cell) type is very poor, though occasional good results are achieved On the other hand, the outlook in the squamous cell variety is relatively good[5–8] There is more doubt about the prospects with an adenocarcinoma, KIRKLIN and his colleagues,[6] for example, consider that the chances of a successful operation are almost as good as with a squamous cell tumour, whereas HOLMES SELLORS's experience[5] has been that the chances are not much better than in the deadly small cell group The prognosis in the large cell variety is poor, though it is apparently somewhat better than when the tumour is of the small cell type[6] Moreover, squamous-cell carcinoma means more than a better chance of survival after a " curative " operation, for a higher proportion of such growths are amenable to surgery when first diagnosed[6 8] , so that at first sight it seems fortunate that in most analyses of the results of treatment in bronchial carcinoma this variety is commonest But, as BIGNALL has lately pointed out,[9] it is the highly malignant small cell

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1 Churchill E D Sweet R H , Soutter L Scannell, J G *J thorac Surg* 1950, 20, 349
2 Ochsner, A De Camp P T De Bakey M. E Ray, C J *J Amer med Ass* 1952, 148 691
3 Gibbon, J H jun , Allbritten F F jun Templeton, J Y Nealon T F jun *Ann Surg* 1953 138, 489
4 Boyd, D P , Smedal, M. I Kirtland, H B jun , Keller, G E Trump, J G *J thorac Surg* 1954, 28, 392
5 Sellors T H *Brit med J* 1955 i, 445
6 Kirklin J W , McDonald, J R , Clagett O T Moersch H J Gage R P *Surg Gynec Obstet* 1955 100, 429
7 McDonald J R , McBurney, R P Carlisle J C , Patton M L *J thorac Surg* 1951, 22 62
8 Ehler A , Stranahan, A Olson K B *New Engl J Med* 1954 251 207
9 Bignall, J R *Lancet*, April 16, 1955 p 786

tumour which preponderates in necropsy studies, and this discrepancy may be explained by the fact that it is the potentially operable cases which go to the special centres from which statistics of survival rates usually come

It is difficult to get reliable information about the actual proportion of all cases which are suitable for surgery when first diagnosed but it is safe to say that it is depressingly low Can the position be improved? Nothing can be done about the most decisive factor influencing survival—the cell type of the tumour—but there is a chance to reduce the delay between the appearance of symptoms and diagnosis Even so, it is doubtful whether any sizeable improvement in the situation would follow and experience so far suggests that mass radiography[9,10] has no striking contribution to make towards a reduction in mortality Indeed BIGNALL came to the sombre conclusion that, even with the most efficient medical service possible we could not, with present methods of diagnosis and treatment hope for any substantial improvement He suggests that we should aim at more effective palliative remedies and it is only necessary to consider the vast sum of human suffering involved to appreciate the value of any such advances

A Century of Army Pathology

THE story of pathology in the Army is one of small beginnings, big opportunities distinguished achievements, and heavy responsibilities faithfully discharged At the centenary of the service last week there was no lack of great names to honour or fine work to recall but above all there was a sense of this work continuing Nor is it limited or separate from work elsewhere Nowhere more than in pathology is there interchange between Army and civilian medicine, and the mixed gathering at the Royal Army Medical Corps Headquarter Mess on April 27 was evidence of a symbiosis which has been particularly happy and always beneficial

The day was chosen because it was on April 27, 1855 that Dr R S D LYONS, an Irish physician, and his "two able assistants" Dr WILLIAM AITKEN and Dr DOYLE, were sent their instructions on the pathological researches they were to undertake at Scutari among the sick and wounded of the Crimea In his centenary article on the service Major-General SACHS[11] quotes these instructions

> 4 As Morbid Anatomy is of little value unless studied in connection with the history of the disease You and your Assistants will require to visit the Hospital wards in order to become acquainted with the symptoms and characters of the diseases during their progress but you will not interfere with the treatment of the patients. In making notes of the cases, the name of the patient, and the number of his regiment should always be stated as by this means the nature of his duties, and the place where he was first attacked by disease can be more easily ascertained
>
> 6 It is expected that you will not content yourself with the simple dissection of the subject and the demonstration of the morbid parts, but that you will submit them to microscopical examination

Even at this early date in an era when little was known about the staining of tissues the importance of the microscope is usefully emphasised, and the instructions are well drawn. Less understanding was shown by the War Office when for years it blocked the plans made by FLORENCE NIGHTINGALE for a school of military hygiene and when at last, in August, 1860, the Practical Army Medical School was opened at Chatham the first 10 students found bare walls and no equipment Nevertheless it was not long before the school as the Army Medical College at Netley, redeemed its bad start Its professor of pathology from 1860 to 1892, Sir WILLIAM AITKEN F R.S , became the father of military pathology and was to make considerable contributions to medicine through his pupils Thus the roll of his assistant professors includes Surgeon Major TIMOTHY LEWIS (F R.S -elect when he died at 45) Sir DAVID BRUCE F.R.S and Sir DAVID SEMPLE. He was succeeded by Sir ALMROTH WRIGHT, F R.S who in 1903 when the college came from Netley to London was in turn succeeded by Sir WILLIAM LEISHMAN F.R.S In 1914 and again from 1919 to 1921 the chair was was held by Colonel S LYLE CUMMINS

In the decade preceding the first world war the value to the Army of a well-organised pathology service was gradually recognised, and the training of regular Army pathologists proceeded steadily, with research by teams as well as individuals The war saw the development of mobile bacteriological laboratories, hospital laboratories and research laboratories and classical work was done on wound sepsis tetanus, gas gangrene shock, and many forms of infectious disease The war also showed the need for a degree of central direction of all these vital undertakings, and in 1919 the Pathology Directorate was founded at the War Office with LEISHMAN as first director assisted by DAVID HARVEY and A C H GRAY At the same time the Army Pathology Advisory Committee came into being—a body to which Sir FREDERICK HARRIS director general of Army Medical Services paid a special tribute last week. (Among its original members was Dr MERVYN GORDON F R.S who attended every one of the seventy meetings during his lifetime) Under these arrangements development continued and research flourished especially in the 30s In India the pathology service profited greatly from the energy and drive of Major (now Major General) JOHN MANIFOLD Also in India, J S K. BOYD F R.S , made his observations on dysentery bacilli, and L T POOLE worked with H E SHORTT of the I.M.S on the virus of sandfly fever At the Royal Army Medical College MARRIAN PERRY was collaborating with H. T FINDLAY and H J BENSTED on virulent typhoid strains in the production of vaccines and BOYD investigated the dosage and administration of tetanus toxoid

In 1939 the Army had a well developed and efficient pathological service capable of rapid expansion Under the directorship of Major General PERRY, the formation of an Army Blood Transfusion Service was undertaken by Sir LIONEL WHITBY who with such lieutenants as G A H BUTTLE W D'A. MAYCOCK, and G T L. ARCHER made it one of the outstanding achievements of medicine in the war In 1941 Major General POOLE succeeding PERRY as director of pathology, took over a task now made immensely intricate by the requirements of large Forces in widely separate theatres of war and by the need to arrange and assist many kinds of urgent research by

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[10] Ilmot K R, Sokoloff M J *Amer Rev Tuberc* 1954 69 161

[11] Sachs A *J R Army Med Cps* 1955 101 100

many different kinds of group How well that task was performed, by him and his assistant Lieut-Colonel BENSTED, is known to many colleagues in all departments of medicine, who were thankful for his combination of high standards with a receptive mind and readiness to help After his retirement in 1945, the directorship was filled, for shorter periods, by Brigadier BOYD, by Brigadier FINDLAY, and by Major-General SACHS, from whose lecture at the college on April 27 we have drawn many of the facts of this outline Since 1953 the director has been Brigadier ARCHER, who arranged this memorable commemoration and at last week's dinner gave what he called the primary response to the toast of the Army Pathology Service proposed by Sir LIONEL WHITBY This is a toast with which a great many people have reason to associate themselves—even though they may never have heard of the service

Annotations

POLIOMYELITIS VACCINATION

MISGIVINGS about the new poliomyelitis vaccine,[1] lately put into extensive use in the United States, have been aggravated by last week's news that a number of children have fallen ill with paralytic poliomyelitis shortly after vaccination It is reported that 35 children have had paralytic poliomyelitis within a short time of vaccination,[2] and 2 have died Almost all these children had been injected with vaccine prepared by the Cutter Laboratories, of Berkeley, California, and supplies from this manufacturer have been recalled In the States of Idaho and California the immunisation programme has been stopped for the time being In Washington the situation has been examined by a group of advisers, including Dr Salk, and they have recommended that inoculations should continue[3] About 4 million people, nearly all children, have so far had a first injection In this country the Medical Research Council decided on Monday that their trials would not start until fuller reports of the American results were available

There are three possible explanations of what has happened First, the children may have been going to get poliomyelitis anyway, and vaccination was too late to have any preventive action Second, the children may have been carriers of poliomyelitis virus, and vaccination acted as a provoking stimulus in a similar way to pertussis and diphtheria immunisation Third, the vaccine may have contained live virus At present there is not enough evidence to decide which explanation is correct, but the third seems the most likely As there is nothing definite to suggest that vaccine manufactured by other laboratories is liable to produce paralytic poliomyelitis, it may be that the virus in certain batches of the Cutter vaccine had been incompletely inactivated

If it should turn out that the vaccine contained live virus two important questions must be considered. Did the Cutter laboratories follow closely the technique of inactivation by formaldehyde recommended by Salk? It seems unlikely that any firm would knowingly vary the procedure, and if these methods were in fact closely followed the margin of safety of this technique should be re examined In particular, there should be a thorough scrutiny, in a number of different laboratories, of the kinetics of inactivation of all three types of poliomyelitis virus by formaldehyde under various conditions The second question concerns the tests of safety which were applied to this particular vaccine Previously, vaccine had been tested to exclude the presence of live virus by tissue-culture techniques and by intracerebral inoculation of monkeys If the tests carried out on the suspect vaccine were not as rigorous as those applied during last year's vaccination trial, the remedy seems clear Many thousands of children received the Cutter vaccine, so the relatively small number of cases of paralytic poliomyelitis may mean that only a few infective virus particles remained in the vaccine On the other hand, if the vaccine passes the safety tests but is still suspect on the grounds of a statistical analysis of the incidence of poliomyelitis following its use, then we must think again about the safety tests Is it wise to apply the results of tests with scores of monkeys to the vaccination of hundreds of thousands of children? We hope that it will not be necessary to make these further inquiries, and that the postvaccination cases may turn out to be unrelated to the vaccine But at the moment it seems unlikely that the vaccine will escape all blame

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[1] *Lancet* April 23 1955 p 851

[2] *New York Times* May 1, 1955

[3] *Times* May 2 1955

ANÆSTHESIA IN OBSTETRICS

THE advances in anæsthesia in the past few years have usually been accompanied by administrative steps which have made the new techniques available to almost every patient who has to have an operation in this country But this scarcely applies to anæsthesia in obstetrics, and there are good reasons to reconsider the position in this branch of anæsthesia, as was done at a meeting of the section of obstetrics and gynæcology of the Royal Society of Medicine on April 22

There has been some uneasiness about an apparent increase in maternal deaths due to anæsthesia, but this may well be only a relative increase, brought about by a fall in the number of deaths from other causes One danger lies in giving general anæsthesia to a patient who has not been properly prepared for it, the mother is sometimes given food and drink almost up to the last moment, and there is occasionally, after prolonged labour, a gastric atony and a stomach full of fluid, which can remind the anæsthetist of paralytic ileus or intestinal obstruction Again, these anæsthetics are not always given by those thoroughly familiar with the drugs they are using, or with the particular points on which to concentrate during the administration Where anæsthetics are given to mothers in labour, suction apparatus should be close by, and the delivery table should be one which will tip both head up and head down. The head-up position, with the use of a relaxant drug and the passage of a cuffed endotracheal tube, is perhaps the safest method in experienced hands Sometimes induction at least should be carried out in the lateral position

The dangers of general anæsthesia emphasise the case for local or regional analgesia whenever possible. General anæsthetics are essential from time to time, for intra-uterine manipulations such as internal version and manual removal of a retained placenta, but the occasions could perhaps be chosen more carefully General anæsthesia is often adopted without question because it allows every conceivable procedure to be carried out, but in many cases another and safer method might have been equally effective Local and regional blocks have difficulties and dangers of their own, but there are many impressive reports of series in which they have been successfully used Perineal field block is probably the safest for mother and baby properly carried out, it will permit low, possibly mid-cavity, forceps delivery and it is particularly suitable for breech delivery As for domiciliary operations, modern antenatal care has made a high proportion of them straightforward, but the same dangers can threaten At the meeting at the Royal Society of Medicine last month, Dr R B Parker gave statistics from Birmingham which showed that the risk of maternal anæsthetic death was greater in hospital dice than in domiciliary obstetrics The domiciliary thetic is almost always chloroform, with or without The dangers of chloroform are well known and se is sharply condemned on all sides; but many mourn the passing of chloroform from hospital tice, and miss the smooth induction and the bility it affords At present there is nothing which replaces it for those who give most of the anæs ics in hospital obstetrics

seems that there is much useful information to be ined from a wide survey of anæsthetic mortality morbidity in obstetrics, both domiciliary and itutional This should take into account the circum ces of the operation the equipment available (such ipping bed and suction apparatus) and the experience training of the anæsthetist

XERORADIOGRAPHY

is a new form of X ray photography xeroradiography wet chemicals are used to develop the latent photo phic image The process is a photo electric one and s first described by Carlson in 1937 Although it has en in use in commercial photography for some time, edical applications are only now being investigated. e technique depends on the property of a group of bstances, known as semi-conductors, to hold an elec ical charge in the dark but to allow it to leak away when posed to light or X rays Of these substances the ost promising so far investigated is amorphous selenium xerographic plate consists of a metal base on which is posited a layer of selenium 120–150 µ thick. It is otected from light and mechanical damage by a cover milar to an ordinary photographic cassette Before e the plate is charged in a special chamber by a high ltage D C. source, which gives the selenium a positive ectrostatic charge The plate is exposed in the normal ay and the image is developed by spraying a fine wder on the surface of the plate in another light oof chamber The powder is taken up by the surface the plate according to the amount of charge remaining d so an image appears It takes about 10 seconds to arge the plate and about 20 seconds to powder it diographically speaking these times are remarkably ort even compared with those possible by the rapid t processing methods now available and there is the ded advantage that no dark room is required. Indeed whole charging and powdering equipment can be ilt into a trolley 4 ft by 2 ft or less and tucked into any ner of the X ray room or operating theatre Costs problematical but the charging and powdering chine may cost from £200 to £500 and the plates about each and since these can be re used indefinitely the thod offers a cheerful prospect of reducing costs

The quality of the image is a more debatable point. The rograph is rather like an etching in black and white d it is viewed by reflected light To the unaccustomed at least it is more difficult to interpret than e conventional radiograph. The image is of low ntrast, and soft tissue and bones are easily distinguish le on the same plate The powder tends to build up lines along the margins of the more dense parts of the age and this enhances the contrast and the clarity detail Fine wire grids as close as 1200 to the inch can resolved whereas, with normal film detail deteriorates 180 lines per inch[1] At the present stage of develop nt the speed of the xerograph is not all it might be ing about the same as that of non screen film; posures are therefore unacceptably long for the heavier rts of the body Another disadvantage is that a rmanent record can be made only by photographing e xerograph on miniature film or by copying it electri lly; this would be a particular drawback when a ries of radiographs has to be inspected regularly or hen it is likely that one or more films will be needed for future reference Further research into the possibility of using a translucent base, to allow inspection by trans mitted light, and of reducing the exposure required may make the method more useful medically

Much of the work on xeroradiography has been done in this country by W D Oliphant in Edinburgh, and trials of the equipment are well under way From America it is depressing to learn that the method is being considered as a means of replacing stocks of ordinary film fogged by atomic explosions But more cheerful news of the interesting medical possibilities should be coming shortly

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[1] Roach, J F Hilleboe H E J Amer med Ass 1955 157 890

SECOND AID

THE treatment of an injury begins almost as soon as it is sustained The patient himself—or a witness who renders assistance or tenders advice—is his first " doctor " From this haphazard beginning he passes through the hands of successively more experienced helpers until he undergoes definitive treatment His progress may involve a parent an older workmate, a resourceful bystander, a civilian or policeman trained in first aid, the chemist,' a nurse, a doctor a hospital and perhaps ultimately a specialist in traumatic surgery or a team of specialists The more serious his injury the more likely he is to follow this sequence to its end but how far he travels along the line depends also partly on chance and partly on the organisation Many of those who get no further than one of the early stages might have profited if they had been carried at least one stage further There is still much avoidable disability because patients with trivial injuries are not brought to clinics and services which are there to treat them until some complication has set in Of those sent to hospitals well fitted to deal with them some have suffered by delay in the preliminary " filter ing some by well meaning but unenlightened handling on the way, and some because no one appreciated that a patient with a dangerous condition may not look dangerously ill

One particular section of this line is receiving increasing attention, as is well illustrated by two publications from the committee on trauma of the American College of Surgeons[1 2] One is the fifth edition of a monograph on the treatment of fractures the other a new companion to it, is a similar work on the early care of soft tissue injuries The growing realisation of the importance of this second type of injury is reflected in the size of the monograph on it, which is twice that of the other Both combine simplicity brevity and absence of distracting controversy with remarkable comprehensiveness. Both may be accepted as a concise presentation of the most authoritative views in contemporary American teaching Both emphasise the value—often the supreme value—of correct *early* treatment which may lie in the hands of younger and comparatively inexperienced people They are aimed at interns and residents in the hospital who serve their periods in the emergency room " and at all doctors who have to do with the treatment of injuries but there is sufficient indication of the later specialised treatment for readers to understand why initial decisions have a vital influence on the final result

It is neither possible nor desirable for every minor injury to be submitted to highly specialised services. Nevertheless much delay in recovery may be avoided if those responsible for early care are guided to select accurately the more serious injuries and if they are briefed on the best way to deal with these before they are sent on Senior surgeons cannot sit all day in their casualty departments waiting for the next accident but they can make clear their wishes on early treatment and they can inform their juniors of the type of surgery likely to be required later in the day House-surgeons casualty officers, and "interns" usually have a comparatively brief term of office Many casualty departments and accident rooms have a periodicity in the standard of their service which corresponds with the length of the doctor's appointment Continuity of policy among successive holders is difficult to maintain, and these publications could do much to maintain it

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[1] An Outline of the Treatment of Fractures By the Committe on Trauma American College of Surgeons 40 East Erie Street, Chicago 11 Ill., U.S.A 1954. [illegible]

[2] Early Care of Soft Tissue Injuries By the Committee on Trauma American College of Surgeons 1954

ANTI-HISTAMINES AS HYPNOTICS

MANY anti histamine drugs in common use cause drowsiness, and that is usually unwelcome, but Straus et al ,[1] in New York, have tried to decide whether this property can be turned to good account In a controlled experiment they have shown that the anti histamine, methapyrilene hydrochloride, in a dose of 50 mg by mouth, is as effective a hypnotic as 100 mg (gr 1½) of phenobarbitone This work confirms a general clinical impression, but anti-histamine drugs are unlikely to be widely accepted as alternative hypnotics to barbiturates

The experiment is of interest because of the methods employed in evaluating methapyrilene's hypnotic powers It was conducted on the "double-blind" principle, and methapyrilene was compared with a positive control (in this case phenobarbitone) and with a negative control (an inert capsule) The "cross over" technique was used—that is, all patients received all the substances being tested, but different sequences were followed in the various patients The choice of phenobarbitone as a positive control was perhaps unfortunate, for this drug is usually classed as a sedative rather than a hypnotic, and 200 mg (gr 3) of pentobarbitone would perhaps have been a better dose The greatest difficulty in an experiment of this kind is the selection of suitable patients Ideally (for unquestionable results), no one should sleep well after the placebo and all should sleep well after the positive control As the experiment was designed with an evaluation period of three weeks, it was necessary to select patients with chronic insomnia relatively uninfluenced by factors other than the change of medication Obviously the ideal conditions will rarely be obtained in practice, and, in fact, although Straus et al selected their 54 subjects with great care (only male patients were included), 30% showed an excellent response to the placebo The number of variables might have been less if each drug had been given only once to each patient, and if a larger number of patients had been used

The criteria of a night's sleep were the patients' own statements in a standard interview and the observations of a night nurse who shone a flashlight on each patient regularly during the night The nurse's impression of the patient's sleep was consistently better than that of the patient himself Other methods of measuring sleep, notably electro encephalography, were considered but all were rejected as inferior to the simpler tests employed Each night's sleep was classified and scored, and the data so obtained were statistically analysed in considerable detail The conclusion was that, as a hypnotic, methapyrilene was superior to the placebo and about equal to phenobarbitone The refinement of the statistical methods seems scarcely suited to the analysis of data measured on an arbitrary scale, and in the presence of many uncontrolled and often unidentifiable variables But Straus and his colleagues have given a very good example of a carefully designed experiment, and it would be a great advance if all new hypnotics were examined with equal care On the other hand, some may think that the information obtained by an elaborate study like this still falls short of scientific proof, and that the judgment of an experienced clinician, based on the observation of relatively few patients (and perhaps of himself on the night train to Scotland), is still a very good measure of what a hypnotic is really worth

ORTHOSTATIC PROTEINURIA

ORTHOSTATIC proteinuria is a condition in which th urine is normal while the patient is lying down, b contains protein when he is up and about It is usual considered to be a temporary and harmless anomal King,[1] in a study of 4000 cases of proteinuria in th United States army, has put forward the view that i is often permanent and not completely benign Th proteinuria persisted for three years in 131 of 170 cas and many of these gave a history of proteinuria for u to ten years previously These observations agree wi those of Thorp and Wakefield [2] who found that 43 o 64 patients still had proteinuria after six years Th incidence of anatomical abnormalities of the kidneys an ureters in cases of orthostatic proteinuria is unusual high King found that 18 of 56 cases showed rad logical abnormalities by intravenous pyelography, a Young et al [3] have reported a similar proportion

The amount of protein lost in the urine may occas ally be as great as in severe glomerulonephritis. Co centrations of protein as high as 4 g per 100 ml in sin urine specimens have been reported,[4] and Wolman states that the range of concentration in 24 hour spe mens is 15–545 mg per 100 ml, with a mean value o 74 mg per 100 ml The highest level corresponds to protein loss of about 8 g daily, equalling that found i many examples of the nephrotic syndrome Elect phoresis showed that the proportion of globulin w unusually high [1]

There is still controversy about the cause of th condition Sonne [6] considered it was the result of c pression of the left renal vein as it crossed the abdom aorta, and Bull [7] thought that rotation of the li during lordosis compressed the inferior vena cava a so increased caval venous pressure King believes th further experimental evidence is necessary before eith of these hypotheses can be accepted King and Baldw have confirmed Bull's finding [7] that there is a profou fall in glomerular filtration rate and renal plasma-f in the erect lordotic posture, but they found no signific difference in filtration rate or plasma flow when c of orthostatic proteinuria were compared with n proteinuric controls

The immediate prognosis in cases of ortho proteinuria is good, and it is certain that this anom does not indicate rapidly progressive renal dis Insurance statistics suggest, however, that the mortal over many years is significantly greater than in cont "good life" cases Daley [9] states that actuarial statis published in 1938 showed a mortality in 52,000 cases "intermittent" proteinuria of 128% of the expect level Further experience [1] up to 1951 suggests t the mortality rises to 150% of the expected figure that the extra deaths are most commonly due cardiovascular disease

THE next session of the General Medical Council open on Tuesday, May 24, at 2 P M, when Sir Da CAMPBELL, the president, will deliver an address. T Medical Disciplinary Committee will meet on Thursd May 26, at 10 30 A M

Prof G W CORNER of Baltimore has been elected foreign member of the Royal Society in recognition his work on the endocrine control of gestation especially on the function of the corpus luteum mammals

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[1] Straus [illegible] Eisenberg J Gennis, J *Ann intern Med* 1955 42, 5

1 King S E *Ann intern Med* 1955 42 296
2 Thorp, E G, Wakefield F G *Ibid* 1933 6 1564
3 Young H H, Haines, J S Prince, C L *Milit Surg* 1
 92 353
4 Hopper J Bolomey A, Wennesland R *Ann intern*
 1954 41 18
5 Wolman I J *Amer J med Sci* 1945, 210, 86
6 Sonne C *Z klin Med* 1921 90 1
7 Bull G M *Clin Sci* 1948, 7 77
8 King, S E, Baldwin, D S *Proc Soc exp Biol* N Y 19
 86 634
9 Daley R M *Urol cutan Rev* 1942, 46, 13

Special Articles

CANCER

THE PSYCHOLOGICAL DISEASE

MALCOLM DONALDSON
FRCS FRCOG
IRECTOR OF CANCER SURVEY YORKSHIRE COUNCIL, BRITISH
EMPIRE CANCER CAMPAIGN

THE title of this article is not intended to suggest hat cancer is a 'psychosomatic' disease but rather o point out that besides the physical disease of cancer here is a psychological condition of 'cancer appre ension,' which affects almost the whole population his mental attitude is present in many members of the edical profession although in their case it assumes rather different form and the fact that discussions n cancer education often generate more heat than rguments about politics or even religion, may in itself e additional proof of my thesis.

PREVALENCE

Is this apprehension of direct harm to the community? learly in its acute form of 'cancerphobia' it causes eat harm to some individuals and each year a few icides are recorded, where the unfortunate victim found to be without trace of the disease Mental orry even if only intermittent as is often the case in ncer apprehension must also be harmful to the indi dual, and, if widespread, must surely be bad for the mmunity What evidence is there that cancer appre nsion is widespread? There is no statistical evidence t surveys in America are suggestive and a survey mong 1200 Manchester women[1] showed that three-arters considered it the most alarming of all diseases

Every doctor has patients who visit him with vague mptoms, and if at the end of an examination the ctor says 'I am glad to say that I can find nothing ious, no evidence of tumour or cancer' as often not the patient will say "Thank God, that was what was really worried about" Such cases clearly indicate e presence of cancer apprehension Unfortunately ne of these cancer-apprehensive patients are not ognised they are labelled neurotics or neurasthenics d they continue to live on the doctor's doorstep in the pe of being reassured

Reluctance in the dislike to mention the word cancer also evidence of apprehension Obituary notices er to a 'long and painful illness bravely borne eart-disease with its greater mortality is never nned in this way) Doctors even if they are not xious about themselves are anxious that nobody ould hear or think about cancer Whether a tient should be told the truth must depend on circum nces. Often the relatives are told but the patient deceived—if he or she can be deceived which is doubtful ter if the relatives think they have cancer the doctor ds it hard to convince them that there is no cancer the Manchester survey already mentioned 40% of e women thought that the patient should be told y attempt to keep the disease 'hush hush' must d, because it is met with so frequently Each year in this ntry about half a million are added to the number people who have already come in direct contact th a patient

An incident illustrating the fatalistic and defeatist titude of some doctors towards cancer happened to e When I entered hospital to be investigated for a ssible gastric carcinoma one of my colleagues said Of course you know you have not got a carcinoma you would never go into hospital On leaving hos tal after an exploratory laparotomy which fortunately oved negative another colleague said 'Of course you were the only person who thought it might be carcinoma Would these remarks have been made about any other disease?

Though there may be a difference in opinion as to how widespread is cancer apprehension there is no doubt that it often delays diagnosis There are no figures to show how many patients put off a visit to the doctor for fear that the condition may be cancer but the answers given in the Manchester survey to the question why women are more frightened of getting cancer than any other disease, are probably also the reasons for delay in reporting symptoms to a doctor Of these the answers that it is 'fatal' 'incurable' 'gets worse' 'only know when it is too late,' and "because of the pain and suffering" head the list

There are figures, however which show the time that elapses after a patient has noticed a symptom before he or she seeks advice Stocks[*] reported that the median number of months interval between the earliest symptom and the start of treatment for cancer of the uterus was 5 7 months (taken from the figures supplied by twenty six hospitals), for the breast 6 months and for the rectum 5 6 months Figures collected by the Yorkshire council of the British Empire Cancer Campaign show much the same delay

TREATMENT

What can be done to lessen apprehension and thus obtain earlier diagnosis? Surely the answer can only be to educate the public by giving information about the accessible cancers and by encouraging people to talk about cancer, and thus to bring their fear to the surface and to face it Those who oppose this plan do so chiefly on the grounds that attempts to educate the public will increase cancer apprehension and fear If true this would certainly defeat the object of obtaining earlier diagnosis Psychiatrists could help us to settle this question, but unfortunately, though interested in the treatment of true 'cancerphobia' patients they have little time to study the problem.

The Yorkshire Council of the B E C C, with the help of some of the local health authorities in the area, have lately given 220 lectures to the public on cancer educa tion At the end of most of these a printed slip is passed to each member of the audience asking whether the lecture has increased their worry and such lectures should not be given or whether it has diminished their worry and more lectures should be given The results from 5740 votes shows 99 1% in favour 0·2% against while 0·7% put a question mark

The other argument used against cancer education is that even if patients are persuaded to visit their doctor when a symptom is noticed the number of cancers treated in the early stage will not be greatly increased because of the large number of growths that disseminate before giving rise to symptoms It is very doubtful whether this is true of the accessible cancers which are the only ones that cancer education can hope to benefit

Figures quoted in support of this are usually based on the results of treatment within six months of noticing symptoms and after six months This is, in fact a comparison between two different types of growth The first set of figures includes all the rapidly growing tumours as well as the slow growing well-differentiated tumours whereas the second set includes only the well differentiated, slow growing ones The figures needed are those for 0–1 month 1–2 months 2–3 months &c., for the accessible cancers In the Manchester survey 76% agreed that there should be freer public discussion of the symptoms

If the psychiatrists could confirm the psychological benefit of cancer education it would be a great help to those of us who are trying to obtain earlier diagnosis

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[1] Paterson R., Aitken-Swan, J *Lancet* 1954 ii 857

[*] Stocks P Studies on Medical and Population Subject No 3 H.M. Stationery Office 1950

WORK OF A GERIATRIC UNIT

A SURVEY OF 13,500 PATIENTS

KENNETH B GIBSON
M.B E , M D Lpool, M.R C P
LATE PHYSICIAN SUPERINTENDENT, NEWSHAM GENERAL HOSPITAL, LIVERPOOL

I HAVE recently completed a survey of all inpatients treated in the 18 medical geriatric wards of this hospital, from the beginning of 1950 to the end of June, 1954 Of these 13,500 patients, 11,000 were over sixty years of age, and some of the findings seem likely to interest others concerned with planning hospital care for the elderly

The Background

Newsham, like many of the country's larger hospitals, had a humble origin as a 19th-century poor-law institution As time went on, buildings designed as dormitories for the able-bodied gradually came to be used as wards for the growing number of infirm inmates The occupants of these wards were mostly old and bedfast Some were merely frail and homeless, some were disabled by chronic disease, some were acutely ill For several decades there were few facilities for medical investigation, treatment, or rehabilitation , but a high standard of nursing care, provided by a hard-working though largely untrained staff, tended to conceal the defects of the system These defects were aggravated and became more conspicuous during the second world war, when a depleted staff had to meet the additional demands of the Emergency Medical Service Its new rôle as an emergency hospital led to the appointment of its first two resident medical officers, but the war precluded any large scale improvement

In 1946 there began a phase of development which has continued ever since, with a minimum of interruption due to the change of management in 1948 Staff was augmented , equipment was provided , and, despite financial restrictions and material shortages, some modest but useful structural alterations have been achieved The original programme for the modernisation of the hospital's 34 wards is now nearly complete, and ancillary services have been steadily expanded to meet the increasing demand for investigation and rehabilitation of a medical staff which now numbers 36 At the beginning of the period of this survey there were already adequate facilities for radiology, pathology, physio therapy, and occupational therapy , and an almoner's department dealt with social problems By the end, all these departments had been further improved and ma new ventures had been started—e g , there was a chirop dist, a dispensing optician, and a cardiographer, t hospital had its first operating-theatre , and a sm follow-up clinic had been set going

The number of beds in medical geriatric wards inev ably fluctuated during four and a half years, and th over all result was a slight reduction from about 740 i 1950 to 707 in 1954 For instance, 16 beds were lo when part of a male ward was converted to enlarge th X-ray department ; others were sacrificed to mu needed sanitary improvements in several wards In t review I have excluded 2 wards for senile dement a 1 mixed psychiatric ward Also I have ignored int departmental transfers , but this two way traffic is to small to influence the main findings

Most of the patients in the survey were admitted a the request of their own general practitioners Dur the greater part of each year there is a waiting list, a patients are admitted in their turn unless their doct ask for priority Apart from an occasional need to a the relative urgency of claims for priority, there was n selection or screening of admissions by the hospit medical staff About 9–10% of each year's admissi were transfers from hostels and other hospitals

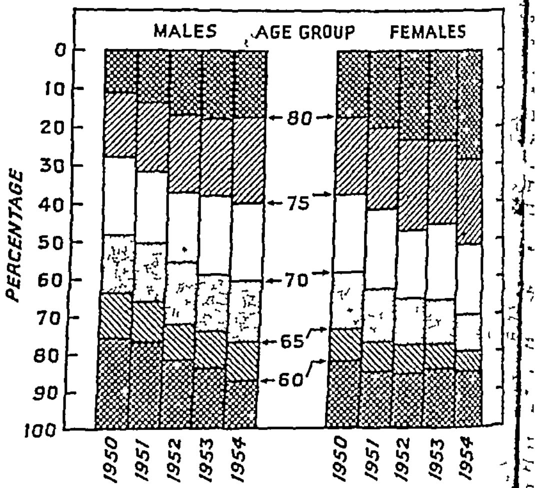

Fig 2—The changing age-distribution of men and women admit geriatric wards in 1950–54 (1954 percentages based on adm during the first six months of the year)

The 18 wards included in the survey form a compo geriatric unit, which undertakes not only investigati treatment, and rehabilitation, but also the long te care of patients with chronic disease who cannot adequately nursed outside hospital The latter are segregated in a separate annexe In general, a wa or group of wards, retains its own long stay pati but tends to concentrate them as a matter of conveni This system is largely dictated by local conditions offers many advantages Both medical and nursing share the variety and interest of different types of wo and most elderly patients like to remain with the s staff throughout their stay Moreover, the atmosph of an active ward helps to sustain an expectation ultimate discharge in the minds both of patients their relatives

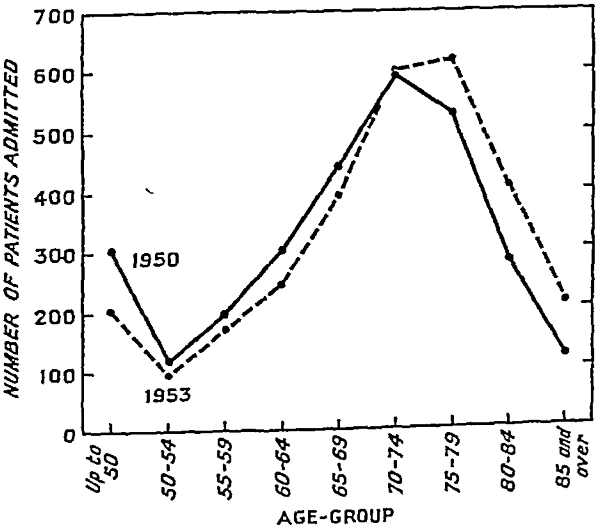

Fig 1 [illegible] of the ages of patients admitted in 1950 and 1953.

Analysis of Results

Age of Patients

Patients over seventy years age of increased fr 1516 (52 8% of all admissions) in 1950 to 1822 (6 in 1953, and represented 65 2% of all patients adm in the first six months of 1954 Higher in the age-s the proportion of admissions over eighty years of a increased from 13 9% in 1950 to 23 2% in 1953 (fig 1

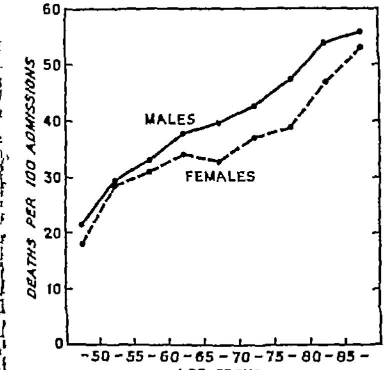

Fig. 3—Mortality of whole series at different ages.

Like other geriatric units (Thomson 1949, Morton 1952, Amulree et al. 1952, Andrews and Wilson 1953) we found that men tend to be admitted at an earlier age than women (fig. 2). In both sexes the age on admission rose in successive years, but women showed a greater increase than men. The increasing proportion of men in the older age groups depended partly on a reduction in the proportion under sixty years of age, while the numbers of women under sixty varied very little.

Mortality

As in the general population, mortality increased with age after fifty years, and in every age group women had a lower mortality than men (fig. 3). Death rates per 100 admissions varied from 18·0 (women under fifty) to 55·4 (men aged eighty five and over); the death rate did not pass the 50% level until age eighty for men and eighty five for women.

Despite the increasing age of patients admitted, mortality rates fell during 1950–53. Annual rates per 100 admissions (table I) are convenient for comparison, though not all the patients dying in a given year were admitted in that year. The mortality of both sexes combined shows a fall in each year after 1950, with the exception of 1951. (This interruption of the downward trend seems to have been caused by a severe influenza epidemic in January and February of that year. Mortality in this epidemic was particularly high in the elderly, and the hospital is situated in an area which was badly affected.) But table II shows that the combined mortality rates conceal an important sex difference. The over-all decline in mortality depends entirely on a fall in female rates (from 38·2% in 1950 to 33·4% in 1953), which offset a smaller rise in the male rates (from 39·5% in 1950 to 42·8% in 1953). The general increase in male mortality depends almost entirely on younger patients, however, for in the death rates of men aged sixty and over the rise is less definite. An unexpected finding was that both sexes had a falling mortality in the seventy-five and over age group. For this group the death rates per 100 admissions were:

TABLE I—MORTALITY IN GERIATRIC WARDS, 1950–53

Year	Patients of all ages			Patients aged 60 and over		
	Admissions	Deaths	Death rate	Admissions	Deaths	Death rate
1950	2877	1121	39·0	2256	963	42·6
1951	3216	1301	40·5	2587	1136	43·9
1952	3017	1166	38·6	[illegible]	1034	41·0
1953	2922	1109	37·9	2450	995	40·6

	1950	*1951*	*1952*	*1953*
Men	50·5	48·0	50·3	50·1
Women	48·5	47·0	41·5	39·5

Turnover

The highest annual total of admissions was 3216 in the year 1951—an increase of 339 over 1950. Rather more than half this increase in turnover can reasonably be attributed to the influenza epidemic, for in 1951 there were 173 more discharges as well as 180 more deaths than in 1950. Admissions then declined to 3017 in 1952, and again to 2922 in 1953. Even in 1953, however, admissions and discharges remained higher than in 1950, and the downward trend appears to have been checked in 1954, for 1523 patients were admitted in the first six months of that year.

The decline in turnover between 1951 and 1953—a difference of 294 admissions—certainly cannot be explained by the small reduction in beds already mentioned; for a loss of 24 beds would account, at 1953 rates of turnover, for 138 admissions at most. But this type of calculation over-simplifies a controversial issue. On the one hand, some of the improvements obtained in exchange for lost beds might be expected indirectly to increase turnover. On the other hand, any reduction in beds will tend to reduce admissions, and improvements, while they may at once increase comfort or convenience, will not increase turnover until this deficit is made good.

TABLE II—COMPARATIVE MORTALITY OF MEN AND WOMEN PATIENTS

Sex	Year	Patients of all ages			Patients aged 60 and over		
		Admissions	Deaths	Death rate	Admissions	Deaths	Death rate
Men	1950	1588	628	39·5	1200	534	44·5
	1951	1716	696	40·6	1316	596	45·3
	1952	1516	617	40·7	1238	538	43·5
	1953	1418	607	42·8	1187	536	45·2
Women	1950	1289	493	38·2	1056	429	40·6
	1951	1500	605	40·3	1271	540	42·5
	1952	1501	549	36·6	1284	496	38·6
	1953	1504	502	33·4	[illegible]	459	36·3

Table III suggests that the decline in admissions during these years depends mainly on falling mortality. The decrease in deaths was almost twice as great as that in discharges; moreover, if each is expressed as a rate per 100 admissions, the death rate fell by 2·6% while the discharge rate increased by 2·3%.

These findings illustrate an unpalatable truth—and a growing problem. Not every patient whose life is saved in a geriatric unit can be discharged, and falling mortality is likely to reduce the number of patients who can be served by each geriatric bed.

The numbers of discharges quoted above include patients transferred to hostels and other hospitals. In 1951, 337 were transferred, but in 1953 only 266, and their corresponding rate per 100 admissions fell from 10·5 to 9·1%. In the same period, patients discharged to their own homes showed a smaller reduction in actual

TABLE III—TURNOVER

Year	Admissions	Discharges		Deaths	
		Numbers	Rate	Numbers	Rate
1951	3216	[illegible]	59·9	1301	40·5
1952	3017	[illegible]	61·4	1166	38·6
1953	[illegible]	1817	62·2	1109	37·9
Difference 1951–53	−294	−108	+2·3	−192	−2·6

TABLE IV—TRANSFERS AND DISCHARGES

—	1951	1953	Difference
Transferred—			
to other hospitals	81	49	32
to hostels	256	217	39
Total transfers	337 (*10 5%*)	266 (*9 1%*)	71 (*−1 4%*)
Discharged to own homes	1588 (*49 4%*)	1551 (*53 0%*)	37 (*+3 6%*)

numbers and their rate per 100 admissions rose from 49 4 to 53 0% (table IV)

The fall in the transfers to other hospitals presumably reflects the development of Newsham and its growing independence of outside facilities The reason for the fall in transfers to hostels is more complex The number of places in local hostels for the elderly has increased in recent years, yet competition for vacancies seems to increase The turnover in the geriatric wards could probably be slightly higher if there were more hostel vacancies But the main problem arises from patients who, even after all possible active treatment, cannot be discharged to their own homes and are too frail to be transferred to most hostels of existing types It is an encouraging sign for the future that locally, at least, the need for a more sheltered type of hostel is recognised, and the hospital is collaborating with both the Liverpool public-health department and the Liverpool Personal Service Society to augment " half-way " accommodation for " frail ambulants "

Length of Stay

The study of length of stay in geriatric wards is complicated by a few patients who remain for long periods and whose final length of stay was still unknown when this survey was made For example, 56 patients admitted in 1949 or earlier, and a further 23 admitted in 1950, still occupied geriatric beds at the end of 1953 I have therefore divided all admissions into two groups —long term patients who stayed over twelve months, and those who left hospital within this arbitrary limit of twelve months According to this classification, 2 5% of the men, 5 2% of the women, and 3 8% of both sexes admitted in 1950–52 were long-term patients The proportion of each sex increased with age, and in every age group women show a higher proportion than men (table v)

TABLE V—PATIENTS ADMITTED 1950–52 WITH LENGTH OF STAY EXCEEDING TWELVE MONTHS

Age	Men	Women	Total
Under 60	15 (*1 4%*)	23 (*3 4%*)	38 (*2 2%*)
60–69	31 (*2 4%*)	36 (*3 8%*)	67 (*3 0%*)
70–79	52 (*2 9%*)	91 (*5 1%*)	143 (*4 0%*)
80 and over	22 (*3 3%*)	74 (*8 4%*)	96 (*6 2%*)
Total all ages	120 (*2 5%*)	224 (*5 2%*)	344 (*3 8%*)
Total 60 and over	*105 (2 8%)*	*201 (5 6%)*	*306 (4 2%)*

Fig 4 shows the proportion of long-term patients of different ages in 1950, 1951, and 1952 Though the proportion to total admissions remains about the same, there is a gratifying fall in the numbers and proportion of patients of seventy-five and over staying longer than twelve months

Admitted in 1950	63 patients (*7 0%*)
" " 1951	60 " (*5 1%*)
" " 1952	50 " (*4 0%*)

Choosing 1951 as an example, and excluding all long-term patients admitted in that year (4 1% of total), I have shown in fig 5 the mean duration of stay of all other patients—i e , those who left the unit within twelve months In this group, again, there is a remarkably close correlation between age and length of stay Both sexes show a steadily increasing length of stay in cessive age groups, but in every group the average of women was longer than that of men These patients also provide information about the effect on turnover of changes in mortality In each sex the average stay before death was much shorter than that before discharge (table vi)

A few of the patients admitted in each year of the survey are still in hospital, and it is not yet known to what extent they will influence the average stay of their group As an example of the serious distortion of average values which can be caused by a small minority of long stay patients, table vii shows the average stay of long term and other patients who left the unit in 19 Of the 3226 patients who died or were discharged, 31 had an individual stay of less than twelve months and the average stay was 47 days, while 121 long-term patients had stayed for an average of 970 days, or more than two and a half years A minority of 3 8% long-term patients raised the average stay of the 96 2% majority from 47 days to 81 days, and accounted for nearly 45% of the quarter million patient days spent in hospital by the whole group

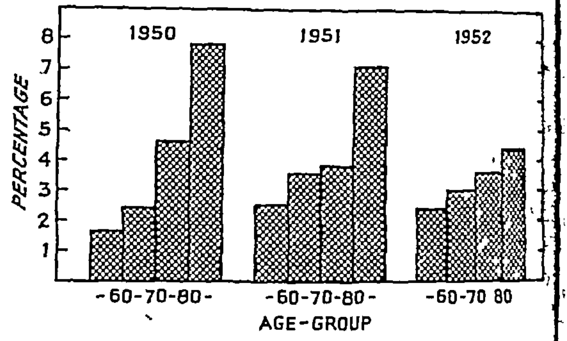

Fig 4—Proportion of each year's admissions with a stay exceeding twelve months, 1950–52.

Use of Beds

An important group of long term patients fails to qualify for inclusion in the usual statistics of admissions, discharges, and deaths in any one year In 1950, for example, 187 beds were occupied throughout the year by patients who were admitted before Jan 1 and remained on Dec 31 The number of beds occupied throughout a whole year fell to 170 in 1951, but rose

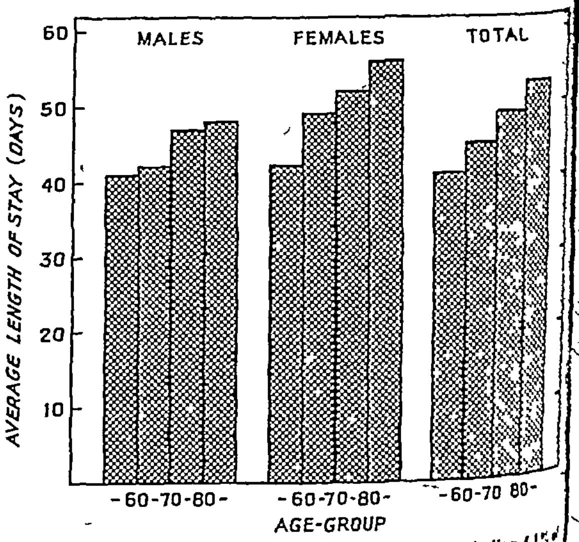

Fig 5—Average stay of patients admitted in 1951, excluding 4 1% total who remained longer than twelve months

ABLE VI—LENGTH OF STAY BEFORE DISCHARGE OR DEATH

—	Average stay (days)					
	All ages			Aged 60 and over		
	Males	Females	Total	Males	Females	Total
fore discharge	6[illegible]	54	53	56	57	56
„ death	33	46	39	32	46	39
ll patients	44	51	47	45	52	48

98 in 1952, and to 201 in 1953 Women patients caused lmost the whole of the increase

It is true that most elderly patients occupy beds little onger than younger patients (Graham 1951 Amulree t al. 1952) Almost half (49%) of the patients leaving he unit in 1951 stayed less than one month and 85% ad an average stay of less than one month Yet even small proportion of long-stay patients in the intake f successive years can cause serious cumulative obstruction of beds. Although only 3 8% of all patients admitted n 1950–52 stayed longer than twelve months more than 8% of the unit's 707 beds were occupied throughout 1953 by long term patients admitted before Jan 1, 1953 f the 201 patients who occupied beds throughout 1953, 141 were women (who occupied 35% of 399 beds in emale wards) and only 60 were men (who occupied 19% the unit's 308 male beds) Table VIII shows that 145 oth sexes) had been admitted in the years 1950–52 d 56 in earlier years before the survey began 14 had mpleted ten years stay by the end of 1953 of whom were under sixty years of age at the time of admission a reminder that younger victims of chronic disease o need hospital beds for long periods

ABLE VII—AVERAGE LENGTH OF STAY BY A SMALL MINORITY OF LONG-TERM PATIENTS BASED ON PATIENTS LEAVING GERIATRIC WARDS IN 1951

Classification by age and length of stay		Number of patients	% of total	Total patient days	Average stay (days)
All ages	Under one year	3105	96·2	145 640	46·9
	Over one year	121	3·8	117 326	969·6
	Total	3226	100·0	262 966	81·5
Aged 60 and over	Under one year	2474	95·8	118 120	47·8
	Over one year	110	4·2	99 476	904·3
	Total	2584	100·0	217 596	84·2

About a third of all long term patients leaving the nit between Jan 1, 1951 and Dec 31, 1953 were ischarged or transferred:

	Discharged	*Died*	*Total*
1951	41	80	121
1952	37	73	110
1953	31	68	99
Total 1951–53	100	[illegible]21	320

hese proportions of discharges and deaths give a somehat gloomy but far from hopeless picture of prognosis long term patients

The unequal sex-distribution of the long term patients able VIII) explains most of the apparent difference in the turnover of male and female beds in this series (table IX)

ABLE VIII—LONG-TERM PATIENTS REMAINING ON DEC 31 1953

Year of admission	Males	Females	Total
1952	22	49	71
1951	13	38	51
1950	6	17	23
1949	6	7	13
1948	3	8	11
1947	3	9	12
1946	—	4	4
1945	—	1	1
1944	—	1	1
Before 1944	5	9	14
Total	60	141	201

Demand for Beds

The demand for the unit's beds can be assessed from waiting lists, which have been counted weekly since the beginning of 1951 (table X)

The long waiting lists created by the influenza epidemic in the first quarter of 1951 were virtually cleared by the autumn of that year Thereafter the total numbers waiting in any one season show a steady increase. Once again however, this increase is not evenly distributed between the sexes Men show a slight increase but their rising trend appears to have been checked in the first part of 1954 Women show a greater and more consistent increase from October, 1951 to June 1954 In 1951 male and female waiting lists were about equal, but in 1953 the female list was almost twice as large as the male list

TABLE IX—ADMISSIONS PER BED IN 1953

—	Males	Females	Total
Number of admissions	1418	1504	2922
Number of beds	308	399	707
Admissions per bed	4·60	3·77	4·13
Beds blocked throughout the year	60	141	201
Beds available for admissions	248	258	506
Admissions per available bed	5·71	5·83	5·77

The major deficiency at present is clearly in female beds 90 have been made available in a newly opened hospital, administered by the same management committee and it is planned to increase this accommodation to over 250 beds within the next twelve months.

Discussion

Many social changes contribute to the growing demand for institutional care of the elderly but the basic cause is the changing age distribution of the population The Royal Commission on Population (1949) taking the year 1947 as a datum line and assuming a falling mortality, estimated that people over sixty five years of age would show an increase of 20% by 1963 and of 64% by 1977 The latest statistics show that in 1947–52 these age groups did in fact increase by 7 7%—an annual rate of 1 5%—which is in close agreement with the estimate Of even greater importance to the hospital services is the redistribution within the age structure of these older age groups Between 1947 and 1952 the number of people aged seventy five and over increased by 14%—almost double the rate of those aged sixty five and over (Annual Abstract of Statistics 1952 and 1953)

TABLE X—AVERAGE WAITING LISTS JANUARY 1951 TO JUNE, 1954 BASED ON WEEKLY COUNTS

Period of year	Males				Females				Total			
	1951	1952	1953	1954	1951	1952	1953	1954	1951	1952	1953	1954
1st quarter	181	66	61	32	133	44	79	111	317	110	140	162
2nd „	21	18	34	34	47	34	65	91	69	49	98	125
3rd „	6	1	[illegible]1		23	8	29		29	9	53	
4th „	3	10	16		9	[illegible]6	66		12	44	81	
Whole year	53	26	33		54	27	60		106	53	93	

In the general population as in the present series, increasing age is more obvious among women than among men In these five years women aged sixty five and over increased by 10% men of the same age by only 4% The sex-difference in the age groups over seventy five is less conspicuous but women show a greater rate of increase than males. Although our local population (Merseyside Conurbation) has a lower percentage of elderly people than the national population there are 173 women to every 100 men of over seventy-five on Merseyside, compared with 162 women to every 100 men in England and Wales (Registrar-General 1952)

The high rate of increase in the age-groups over seventy-five affects the hospital services in two ways First, because among the over-seventies there is a sharp increase in frailty, dependence on others, and demand for institutional care (Sheldon 1950, 1954) For example, the 1951 census returns (1% sample) showed that 48% of men remained in whole-time employment after the age of sixty-five, but only 20% after the age of seventy Similarly, the Wolverhampton survey (Sheldon 1948) showed that the proportion of women undertaking the sole domestic care of their household remained fairly constant at about 50% between the ages of sixty and seventy-four, but declined to 40% after seventy five and to 18% after eighty years As long as morbidity continues at present levels, any increase in these older age groups must cause a disproportionate rise in the demand for hospital beds Lowe and McKeown (1950) calculated age specific rates for patients in hospitals for the chronic sick per 1000 of the Birmingham population their rates show a remarkably sharp increase in the older groups

Age	*Rate per 1000*
55–64	1 53
65–74	6 38
75–84	22 21
85 +	58 93

This survey also suggests that an increase in the age of patients admitted to geriatric beds will tend to reduce turnover—both by increasing the proportion of long stay patients and by lengthening the average stay of those discharged

The Wolverhampton survey drew attention to the fact that the lower mortality of old women is accompanied by a morbidity higher than that of old men, and there has since been ample evidence that the proportion of hospital accommodation required for older women is far greater than can be explained by their greater numbers Greenwood (1949), Exton-Smith (1952), Morton (1952), and Andrews and Wilson (1953) all quote examples of the disproportionate demand for female beds, and in the Birmingham survey women had a higher age specific rate than men at all ages after seventy-five

Estimates of future hospital scales based on the total numbers of both sexes, either in the whole population or in the combined age-groups over sixty or sixty-five years, can have only a short-term reliability Long term planning should take account of the changing age-structure and sex distribution of the older population

The difficulties of long term planning have been discussed in a P E P study (1954), which reviews basic assumptions about trends in birth rates and mortality, and suggests that previous estimates of the economic burden of old age may have been exaggerated Fortunately changes in the birth-rate cannot directly increase the burden on the geriatrician for sixty years or more —though the size of the working population will influence the amount of the national income available for welfare services, including hospitals The future demand on the hospital services will depend both on the numbers of old people alive, and on the incidence of disease among them It is a melancholy thought that many of the problems of old age are a by-product of unbalanced medical progress We can prevent or cure many of the diseases which used to kill we cannot yet control many of the more insidious diseases which disable those who survive into an extended old age The control of arterial degeneration would probably do more than any other scientific advance to reduce the social and economic problems as well as the suffering of old age Extra longevity without lower morbidity is a doubtful blessing for most of us Old age must be made healthier and more useful if it is to be anything but an increasing burden, both to the individual and to the community

It is a pleasure to acknowledge the willing assistance of many members of the hospital staff I am especially indebted to Miss C Ledsham and others who helped in the tedious work of extracting the basic figures for this survey

REFERENCES

Amulree, Lord Arnold, P, Polak A (1952) *Lancet*, ii, 191
Andrews, C T, Wilson, T S (1953) *Ibid* i 785
Annual Abstract of Statistics (1952 and 1953) H.M Stationery Office
Exton-Smith, A N (1952) *Brit med J* ii, 182
Graham, W L (1951) *Lancet*, ii, 931
Greenwood, J M. (1949) *Ibid* ii 1047
Lowe C R, McKeown, T (1950) *Brit J soc Med* 4, 61
Morton W (1952) *Brit med J* ii, 715
Political and Economic Planning (1954) No 364, see *Lancet* 1954, ii, 278
Registrar General (1952) Statistical Review of England and Wales H M. Stationery Office
Royal Commission on Population (1949) Report H M Stationery Office
Sheldon, J H (1948) The Social Medicine of Old Age London.
— (1950) *Brit. med J* i, 319
— (1954) *Lancet* ii, 151
Thomson, A. P (1949) *Brit med J* ii, 243

SALARIES IN THE PUBLIC-HEALTH SERVICE

Under an Industrial Court award which operates as from Jan 1, 1955, medical officers of health, senior medical officers, and medical officers in departments (assistant medical officers) are to receive increases in salary ranging from £175 to £200 The new salary scales are as follows

Medical officers of health

Population Group	*Commencing salary*	*Increments*
Not exceeding		
75,000	£1625–£1830	4 × £5[illegible] 10s
100,000	£1730–£2040	6 × £51 10s
150 000	£1940–£2250	6 × £51 10s
250 000	£2150–£2450	2 × £100 1 × £50
400,000	£2400–£2700	2 × £100 1 × £50
600,000	£2500–£2900	3 × £100
Over 600 000	At discretion	At discretion

Senior medical officers

£1415 × 50–£1765 × 65–£1830

Medical officers in departments (assistant medical officers)

£975 × 50–£1375

The court found against a proposal to introduce in Scotland a salary scale for a medical officer of health with a population group not exceeding 60,000

WHOLE-TIME AND PART-TIME CONSULTANTS

The Joint Consultants Committees have had recent discussions with the Ministry of Health and the Department of Health for Scotland about whole time and maximum part time service for consultants in the National Health Service, and the following is an agreed statement of the position

It is recognised that some consultants, while prepared to devote substantially the whole of their time to hospital work and to give it priority on all occasions, would prefer a maximum part-time to a whole time contract Ever since 1948 it has been the Ministry's view that, subject always to the needs of the hospital service, employing boards should in this matter take into account the circumstances and preferences of the consultants concerned While there has been no previous statement on this point as regards Scotland, the practice in that country has been similar

Where a new appointment is being made this means that, except where the board decides that the needs of the hospital service (considered in conjunction with the of the local health services where the consultant is to undertake duties on behalf of a local authority) demand a whole time appointment, the competition should be thrown open to all applicants who are prepared to give substantially the whole of their time to the post, whether they prefer a whole-time or a maximum part time contract In such a case the successful candidate should e asked to state his preference until after he has been elected for appointment

Similarly, if a consultant who is already employed in whole time post wishes to transfer to a maximum part-ime contract, or vice versa the board should, before eaching a decision, take his circumstances and preferences into account again subject to the overriding needs of he hospital service.

This statement does not, of course deal with the many ases where the services of a consultant are needed in the ggregate for only a limited volume of work and where erefore a part time appointment would in all cases be ppropriate.

Public Health

Vaccination in London

At a meeting of the London County Council on April 20 t was stated that the percentage (based on live births) of London children under 1 year vaccinated against smallpox hows a steady improvement since 1949 The figures re as follows:

1949	25%	1951	38%	1953	48%
1950	32%	1952	45%	1954	49%

There is continual propaganda on the part of the ouncil's health visitors and clinic doctors to persuade others to have their young children vaccinated General ractitioners are encouraged to take their part in vaccina on and are paid a fee of 5s for each notification sent to e council. Opportunity is also taken to encourage accination by the distribution of literature and display f appropriate material in council establishments

Notification of Tuberculosis

A recent Ministry of Health memorandum[1] explains which medical officer of health should be notified when a erson is diagnosed in hospital as suffering from tubercu sis. Notifications should usually be sent to the medical fficer of health of the district in which the patient ormally lives; but where in the case of long-stay atients, the hospital itself can reasonably be regarded s the *patient's place of residence the notification should* e sent to the medical officer of health of the district in hich the hospital is situated.

Swedish Poliomyelitis Vaccine

As we reported a fortnight ago[2] plans are going ahead Sweden for the use of a poliomyelitis vaccine made growing virus on human tissue Further details have en given in a report by Prof Gunnar Olin of the edish State Bacteriological Laboratory The virus as been grown on aborted human fœtal tissue, and then activated with formalin (1 in 2000 compared with the in 4000 formalin recommended by Salk) The inacti ation is performed at 25 C (the American workers efer 37°C) The antibody response is said to be good hough vaccine has been prepared to immunise 120 000 hildren, but further supplies may be limited by the hortage of suitable tissue for culture American vaccine ay be imported for the time being

Education of Physically Handicapped

The Ministry of Education[3] has found that on Oct 1 31 1052 children were awaiting places in special schools. heir disabilities were as follows: cerebral palsy 485 liomyelitis 100 heart defects, 78 muscular dys-ophy 78; spina bifida, 68 hydrocephalus, 42 formities, 40; hæmophilia 20 fragilitas ossium, 20 berculosis 10; Perthes's disease 12 muscular atrophy, rheumatoid arthritis, 3; others, 83

Of the 1052 children 202 were awaiting places in day hools and 850 in boarding schools. The existing ucational arrangements for these children were as llows: 371 were receiving home tuition 250 were ordinary schools; and 100 were receiving some other pe of special educational treatment (mainly in hos itals). Of the 725 unprovided for some were not receiving home tuition because of difficulty in finding teachers or of unsuitable home conditions

There appeared to be enough places in day special schools There is still a shortage of places in boarding schools but additional places expected to come into use within the next two or three years should suffice for all children whose parents are likely to consent to their attending such schools

First Quarter in England and Wales

The Registrar General, in his provisional figures[1] for England and Wales in the first quarter of 1955, records a birth rate of 15·5 per 1000 population, compared with 15·9 per 1000 in the first quarter of 1954 The death rate was 15·4 per 1000 population, as against 14·0 per 1000 in the first quarter of 1954 The infant-mortality rate was a new low record for a March quarter—29·0 per 1000 related live births It was 31·0 per 1000 (the previous record) in the first quarter of 1954 The stillbirth rate was 23·1 per 1000 live and still births compared with 23·7 in the *corresponding quarter of* 1954

Parliament

Disseminated Sclerosis and War Pensions

In the House of Commons on April 20 Mr ARTHUR MOYLE asked the Minister of Pensions and National Insurance to examine the rules and the present terms of the Royal Warrant to see whether ex-Servicemen with disseminated sclerosis might not be assessed at the 100% disability rate—Brigadier J G SMYTH joint parliamentary secretary to the Ministry pointed out that in the first world war two-thirds of the casualties were wounds In the second world war the causes of two thirds of the pensionable cases were diseases. But to earn a war pension these diseases must be causally connected with service *There was no evidence that* disseminated sclerosis was in any way a military disease. The Ministry tried, however, to stretch the regulations as far as they could and where a man had been subjected to a sudden shock, and within a short period showed signs of disseminated sclerosis they said that perhaps the shock, although they knew it had nothing to do with the disease had accelerated its progress and pensions were granted for aggravation Accordingly after the late war pensions for aggravation of disseminated sclerosis were awarded in 1538 cases and there had been 1117 rejections.

QUESTION TIME

Ban on Heroin Imports

In the House of Lords, replying to a question Lord MANCROFT said that except for small quantities for purely scientific purposes Her Majesty's Government had decided not to permit the manufacture and export of heroin after Dec 31, 1955 As adequate supplies had hitherto been manufactured in this country imports of heroin had not been authorised for many years: it was intended to maintain the prohibition on importation. The Government had taken this decision in order to give effect to a resolution adopted by the Economic and Social Council of the United Nations at its 18th session, urging all governments to prohibit the manufacture export, and import of this drug except for scientific purposes. Before the *decision* was reached the advice of the appropriate statutory advisory bodies was taken.

Viscount ELIBANK Are the Government aware that Dr Arthur Douthwaite senior physician at Guy's Hospital, has stated in the *British Medical Journal* that the banning of this pain killing drug heroin, is an astonishing move which will inflict much hardship upon a multitude of patients? Is the noble Lord aware that one of the best known physicians in Edinburgh, Dr A B Flett has written to me saying it is iniquitous that this most useful, and often, in certain cases really necessary drug should be banned?—Lord MANCROFT: The Government are aware of these opinions On the other hand I understand that adequate supplies of perfectly good substitutes for this drug are now available The purpose of the action is, of course to facilitate the world wide banning of traffic in this extremely dangerous drug

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[1] HM(55)33.

[2] *Lancet* April 23 1955 p 857

[3] Ministry of Education: administrative memorandum no. 503 April 25 1955

[1] Registrar-General weekly return no 15 1955 H.M. Stationery Office 1 p. 20 1s

I do not think that the Government can do more than follow the technical advice and guidance given by the Central Health Services Council, the Standing Medical Advisory Committee, and the appropriate bodies in Scotland and Northern Ireland

Poliomyelitis Vaccine

Replying to questions, Mr Iain Macleod, the Minister of Health, said that a small field trial with the Salk poliomyelitis vaccine was being carried out by the Medical Research Council All vaccine used in this trial, whether imported or manufactured here, would first have been the subject of rigorous tests by the council Plans for large scale immunisation were, of course, dependent on the Minister of Health being satisfied, so far as was humanly possible, as a result of these tests and trials that the vaccine to be used was both efficient and free from danger

Mr Eric Fletcher Would the Minister say whether any supplies of Salk vaccine from the Cutter Laboratories have been received in this country ?—Mr Macleod No Cutter vaccine has been received in this country

Mr Mont Follick Are the vaccines which are being made by the Glaxo Laboratories of their own special prescription, or according to a prescription imported from America ?—Mr Macleod I understand that what they are making is, in fact, the Salk vaccine The difficulties in this case have arisen, I understand, from a batch made by the Cutter Laboratories As we have none from those batches in this country, there should not be difficulty in that particular direction

Salaries of Hospital Pharmacists

Replying to questions Mr Macleod said that a general agreement on increased salaries for hospital pharmacists was reached by the appropriate Whitley Council on April 20 Details were now being worked out

General Practitioners in the N H S

Replying to questions, Miss Patricia Hornsby Smith, parliamentary secretary to the Ministry of Health, said that on July 1, 1954, 19,300 general practitioners were practising in the National Health Service Altogether 837 doctors practised single handed and 614 partnerships employed assistants, other than trainees The Minister of Health was not prepared to limit the increased number on a list when an assistant was employed to a maximum of 1500 The relationship of principals and their assistants could not readily be regulated by statute

Mr Somerville Hastings Does not the Minister realise that many doctors find great difficulty in getting the necessary capital to start in practice and are therefore liable to be exploited by doctors who employ them as assistants ?—Miss Hornsby Smith The matter is being considered by the British Medical Association and the Medical Practitioners' Union, but we have had no decisions or opinions from them yet

Mr H Marquand Does the hon lady recollect that it was a definite promise by the medical profession at the time when the payment to general practitioners was referred to adjudication that they would seek to reduce the number of assistants and increase the number of principals in practice ? Is she satisfied that the medical profession are giving real coöperation in this matter as they undertook to do ?—Miss Hornsby Smith There has been an increase in partnerships and a reduction in the number who do a long period as assistants These consultations are going on between the B.M.A and the M P U and I think the profession are coöperating in this matter where they feel that there is hardship Mr Hastings said that the B M.A. committee had already reported and their report was by no means entirely happy about the situation

Replying to a further question, Miss Hornsby Smith said that on July 1, 1954, 131 assistants were still in posts which they had taken up before July 1, 1949 Mr Hastings Does not the Minister think that this is a serious matter ? Even her own figures show that While it is admitted that doctors may derive a good deal of benefit from being assistants for a time, does she not agree that for them to go on year after year in that position, as these figures suggest, is a very dangerous situation ?—Miss Hornsby Smith I think we should keep this matter in proportion There is a steady increase in the trend towards partnerships Mr Marquand Would it not be possible to make an inquiry into this comparatively small number of cases to see what the reason is for this long period of assistantship ?—Miss Hornsby Smith We will consider that point

Lung-cancer Mortality

Replying to a question, Mr Macleod said that the provisional number of deaths attributed to cancer of the [illegible] 1954 was 16,332 The numbers of deaths so attributed in [illegible] and 1944 were 2775 and 6684

Mr Hastings Does the Minister realise the importance to the health of the community resulting from his pronouncements on this subject some few years ago ? Will he consider making a similar pronouncement setting forth the increased knowledge up-to date resulting from research ?—Mr Macleod I recognise the public anxiety here and I shall be very glad to consider the suggestion Dr Barnett Stross Would it not be true to say that whatever may be the cause of this disease—and many people now suspect what may be the cause—it cannot be the ingestion of any foodstuffs that is causing the rise in cancer of the lung, for it would affect women as well as men, and that it does not do ?—Mr Macleod Whatever may be the reason, it is true that the increase is very much more—indeed it is more than twice as great—amongst men than women, which would seem to indicate a special cause

Child's Treatment in Hospital

Mr Kenneth Robinson asked the Minister why a boy aged 10, who was admitted to Hampstead General Hospital on March 30 with a fractured and dislocated arm, received no medical attention for more than six hours, during which time he was offered neither food nor a sedative —Mr Macleod replied I am very much afraid that the facts are as stated and it is clear that the hospital staff failed grossly in providing proper attention On behalf of the board of governors and myself I must apologise to the child's parents I assure them that the board take a serious view of the whole incident and that those responsible have been severely reprimanded Mr Robinson Whilst I welcome the Minister's admission of the responsibility of the board of governors for the matter, and, of course, accept his assurance of regret, does he not agree that the public has been led to expect that the teaching hospitals should set a standard of conduct in these matters, and does that not make the incident even more deplorable ?—Mr Macleod No doubt that is true I am bound to say that the only thing I welcome about this case is that the hospital at once admitted an error As we know errors happen in the hospital service I deeply regret that this should have happened, and my views have been put very strongly to those concerned Mr Hastings Will the Minister make it quite clear that it is his desire that at every general hospital there should be a medical cover throughout the twenty four hours, and that so many doctors should not be away from their work as at present ?—Mr Macleod It is certainly desirable that wherever possible cover should be provided, if not on a twenty four hour basis, at least urgent and near

Requests for Lists of Patients

Replying to a question, Miss Hornsby Smith said that the Minister of Health was not aware that political party organisations were asking doctors for lists of patients for the purpose of the postal vote at the general election

Mrs Barbara Castle I have in my possession circular letters from Conservative associations to local doctors in their areas asking them to supply the Conservative party with the names of blind, sick, and aged patients on their registers in order that they may be contacted with a view to their having a postal vote Will the Minister institute an immediate inquiry and inform the doctors that this is contrary to professional etiquette and their duty to their patients ?—Miss Hornsby Smith If the hon lady will let the Minister have the evidence I can assure her that he will look into the matter The vote is secret and in their individual capacity it is certainly helpful to see that as many as possible obtain their vote

Mr Herbert Morrison Will the hon lady on behalf of the Minister give an assurance that neither directly or indirectly will those associated with the National Health Service be coöperators with any political party organisation in connection with the forthcoming election ? Is she aware that there was the strongest impression at the last election that such malpractices took place ?—Miss Hornsby-Smith I can certainly give the assurance that the Health Service will not be used in this way

Replying to further questions, Mr Macleod said he would ook into this matter at once Whether he would make a tatement on it would depend on the results of his inquiries.

Orthodontic Treatment

Replying to questions Miss Hornsby-Smith said that he number of courses of orthodontic treatment approved nder the National Health Service for 1949 was 12 000 and he payments made were £300 000 The figures for 1954 ere 48 000 and £500 000 Orthodontic treatment was rovided under the hospital and specialist services, the school ealth service and the general dental services. The number f dentists in England and Wales who in 1954 were each given pproval to start more than 100 courses of orthodontics under he general dental services was 42

Medical Examination of Broadmoor Prisoners

Mr T E Driberg asked the Home Secretary if he was ware that a medical report by the principal medical officer f Brixton Prison dated Feb 14 1953 stated that a prisoner was sane and fit to stand trial on a charge of attempting to murder his wife and recommended him as suitable for voluntary treatment in a mental hospital; that at his trial five days later this man was found guilty but insane and ordered o be detained during Her Majesty's pleasure and that he is till detained at Broadmoor where his wife and other relatives had found him in apparently normal health and if in these circumstances, he would allow an independent medical xamination of this patient.—Major Lloyd George replied The responsibility for deciding when a Broadmoor patient s fit to be transferred or discharged rests on the Home Secretary and my predecessors and I have consistently taken the view that the expert staff of psychiatrists at Broadmoor who have the patient under constant observation are n a better position than an outside doctor to advise the Home Secretary on the patient's mental state and future prospects. The answer to the last part of the question is, therefore No Sir

Mr Driberg Is the Home Secretary aware that Dr Mathieson, of Brixton, also said that this man was suffering imply from a mild anxiety neurosis, which should yield to proper psychiatric treatment but that since he has been in Broadmoor he has had no such treatment whatever? It is obviously impossible for the very efficient and conscientious staff at Broadmoor to give proper psychiatric treatment to the very large number of patients with whom they have to deal. In the circumstances, will the Home Secretary consider either getting an independent opinion r transferring the man to a mental hospital where he can be treated?—Major Lloyd George: These cases are very difficult I am aware of the opinion to which the hon Member has referred and I have of course gone into the case myself with great care On the information I have I do not think anything can be done But I am prepared to look at the matter again and I will do so

Motoring Offences and Blood Tests

Replying to a question, Sir Hugh Lucas Tooth, joint under secretary of State to the Home Office said that during the last ear no motorist charged by the Metropolitan Police with being under the influence of drink while in charge of a car had requested a blood test but in one case samples of blood and urine were taken at the request of a doctor called on behalf of a person who had been arrested for such an offence

Mr Somerville Hastings: Does the Minister not agree that this test which has been largely used in other countries might usefully be tried out in this country so that some idea would be obtained of its real value? At present its value seems to be somewhat uncertain. Will the test be made possible for those who apply for it?

Sir Hugh Lucas Tooth: Opinion about the value of blood tests in these cases is sharply divided, and it would be inappropriate for me to express a view either way at the present time. Research on the effects of alcohol upon driving performance is being carried out by the Medical Research Council and the Road Research Laboratory

Mr R. R. Stokes: Have not the police chucked this bit of nonsense as being absolutely unreliable?

Replying to a further question Sir Hugh Lucas Tooth said that the provisional figures showed that in magistrates courts in England and Wales there were during the first nine months of 1954 1051 convictions of driving or being in charge of a motor vehicle while under the influence of drink or drug The number of resulting sentences of imprisonment was 112

In England Now

A Running Commentary by Peripatetic Correspondents

They say a psychiatrist is a man who goes to the Folies Bergère to look at the audience, so I went to the Private View day at the Royal Academy The trouble about Private View day is that you get trampled underfoot by people with one eye on the pictures and the other on the look-out for their friends But still, it has the advantage that the ladies hats are more surprising than they are on other days, and the girls seem prettier and you can watch the artists being casual about their masterpieces They have a variety of techniques for this. I heard one ask, in incredulous tones, 'Do you mean you *like* it? but whether this was modesty, or surprise that his audience appreciated it, I could not tell. Then I like to see the subjects standing sheepishly near portraits of themselves. I am one of those people who do not get much further in Art than knowing what they like, but I did like the portraits this year there were several startlingly good ones and very few of those others. I liked the one of the toy monkey because he unlike most of the other sitters, was not pretending to be blase about having his picture painted There were, of course, the usual dreary people sitting in dreary rooms but I wonder how Charles Spencelayh manages to make ordinary objects so exciting? I suspect that the secret lies in the title he has given to one of his groups—*God's Good Things* Perhaps it is because I like bouncy dogs, but I was intrigued by *Whippet* in terra cotta, who had curly ears and a curly tail and was very much alive. 'And ducks are soothy things and lovely on the lake That was another lovely thing in oak, a mother duck obviously telling her brood a bedtime story Exciting in a different way is a statue of a nun, with severe straight lines except for her face and expressive hands. There is so much too much, to take in as always The biggest crowd was consistently round what has now come to be known as the Annigoni of the Queen For the record the most frequent remark I heard in the whole exhibition was The traffic my dear, was simply frightful.

* * *

My medical wife and I discussed the mushrooms fully Growing they were pleasant-looking things and after consulting the encyclopædia we convinced ourselves that they were edible We ate them for breakfast the following day and I had a large helping which tasted delicious with bacon My wife drove me to the hospital where I sat down in the office to attend to some routine papers Some thirty minutes after breakfast the odd feeling started I found it difficult to concentrate on my work and noticed a transient diplopia which could be mastered only by an effort. I experienced a curious sensation of being in the room but apart from my body The voice of someone speaking in an adjoining office seemed a great distance away Of course this disturbed me but the probable cause eluded me for a while. Then—The Mushrooms! I grabbed the phone and with some difficulty dialled my home. With great relief I heard my wife s voice, though it was slurred and not too intelligible. In the brief moments of waiting for her to answer I had an awful vision of her having crashed the car on the way home She too felt very odd and had just realised why By this time I was getting a bit disorientated but I sent one of my colleagues off to bring my wife my daughter, and the lodger into hospital. I then floated rather than walked up to the ward for a stomach pump session. I was given atropine and intravenous glucose and rapidly felt better

My wife who was not treated so soon became quite confused and went into a state of shock before she reached hospital but fortunately retained enough presence of mind to insist on picking up the lodger from her office on the way The three of them were then treated as I was, to the intense indignation of daughter aged eight who had eaten only one small mushroom and felt quite well They too improved rapidly, but my wife remained mildly shocked for several hours

I found it impossible to get the fungus identified but assumed that it was one of the types containing a mus carine-like alkaloid—possibly *Inocybe patouillardi* I don't think it could have been *Amanita muscaria*, which from its pictures seems a distinctive fungus quite unlike our specimens

The story spread rapidly and, needless to say, such an occurrence in a medical family was the cause of much ribald comment The loudest laugh was enjoyed by my son aged twelve who doesn't like mushrooms and who refused them on this occasion because he didn't like the look of them His big moment came when he poked his head into my hospital room and said "I told you so!"

* * *

Some of our West End colleagues still bemoan the loss due to war, the B B C, and Big Business, of the Langham, and now the Bolivar—its posteriorly situated vestigial remnant—has suddenly closed its hospitable doors It is heart-rending to see thirsty pillars of our profession being caught out by padlocked doors without so much as a "closed" notice on them I saw one famous man nip round the corner to check his watch against the All Souls' clock before the devastating truth dawned upon him Where consultants' fluid-balance and milli-equivalents can conveniently be put in order now, goodness only knows What with this calamity and the Med Soc Lond having no visible means of support at its northern end, Chandos Street is not what it was

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Those who heard Pierre Monteux conducting the Royal Philharmonic Orchestra at the age of 80 must have marvelled at his apparently limitless energy Bruno Walter, one year younger, is to take command of the B.B C Orchestra this month It is only a few years since Toscanini, now 88, electrified us all at the Festival Hall Vaughan Williams, at 83, would probably call himself an amateur conductor only Weingartner, Mengelberg, Richard Strauss, and Kussevitzky were all around, or well above, 80 when they died in full harness Sir Thomas, of course, is a mere stripling at 75, he, Cameron, and Ansermet are a trio of active septuagenarians Sir Henry Wood had hardly shed any of his habitual load of work when he died at 75

It is fortunate for the rest of us that these eminent maestros enjoy such long spans But why do they? Is it because, unlike most surgeons and professors, they keep on working? Or are eminence and longevity associated irrespective of occupation? Quite apart from ex-prime ministers, Augustus John and Brangwyn are well into their eighties, Sir Gerald Kelly and Sir Alfred Munnings are in their late seventies

A famous but still relatively young conductor once told me that, while in action, he felt "the vital juices flowing down the arms to the heart" Perhaps he was right, perhaps the apparent immunity of orchestral conductors to the more spectacular forms of cardiovascular collapse is due to the fact that they wave their arms about a good deal

* * *

How much we suffer from failure to convey our wishes correctly to our patients Listening to one's colleagues shows how much time and effort are wasted by lack of liaison

"Lie on your back on the couch—No, on your back, please"

"Show me where the pain comes—No, on your own back please"

"Please stand up—now, raise your right leg—thank you, and now your left leg—thank you, and now get off the floor"

There is clearly an urgent need to revise the technique of medical questioning, and at the next twelve unselected outpatient clinics we are giving a trial to the following phrases

"Lie on the couch with your tummy upwards"
"Show me on your own back where the pain is"
"Bend your knee crooked—and now bend it straight"

I would welcome suggestions how to avoid the inevitable contraction of the calf muscle just as I withdraw the tendon hammer from my pocket "Relax," "Pretend you're asleep," "Don't bother about me," "Go loose," and "Pretend you're dead" have been tried and found wanting

Letters to the Editor

HASHIMOTO'S STRUMA LYMPHOMATOSA

SIR,—Independently, we have each been interested several years in Hashimoto's "struma lyphomatosa" 1953, again independently, we obtained marke abnormal liver-function tests in some of these cas finding of which we have seen no previous record, and which one of us drew attention in your columns year[1] This mutual interest came to light when we by chance on the slopes of a Yorkshire mountain, not having met as colleagues for over twenty years. intend to record our findings in full in due course but preliminary details may interest your readers

Owing to a difference of approach there is some of uniformity in our case records, but we are agreed the main observations

(1) The presumptive diagnosis is essentially clinical the condition is commoner than is generally suppos Although there are certain typical features, includ preponderance of cases in middle aged females, sympto of subthyroidism of variable degree, and a thyroid easily felt and abnormally firm, we would stress that infrequently the patient first visits her doctor for sym toms not quickly ascribed to thyroid disturbance, as lassitude, muscle and joint pains, increasing weig and changed facial appearance The efficacy of mod treatment by oral dried thyroid emphasises the need the diagnosis of Hashimoto's disease to be consider more readily We have studied about 25 patients, nearly two thirds of whom the diagnosis has confirmed by surgical section

(2) The basal metabolic rate is subnormal in most the patients when first seen, but a minority in the stage show signs and symptoms of hyperthyroidi Anæmia is not a characteristic feature

(3) The liver function test most consistently abnor in the untreated patient is the colloidal gold te thymol turbidity and flocculation tests generally parallel with it In a few patients the serum alka phosphatase is slightly or moderately raised T bromsulphalein test may be abnormal, but the galac tolerance has been normal in the 5 patients exami After treatment by dried thyroid gland, the liver-func tests in some patients return to, or towards, nor within a period of months, but in others the retur much slower and we have seen the tests still gro abnormal after more than two years Electrophor shows a raised and abnormal serum-globulin level in few patients In general, however, there appears to no close relationship between the results of the flocc tion test and the plasma cholesterol, or the ba metabolic rate

(4) We suspect that gross liver disease may arise struma lymphomatosa One of our patients, observed seven years, now has a liver which is greatly enlarg and abnormally firm, and a palpable spleen The spl is palpable in 2 of 17 other patients In the 1 patient whom surgical biopsy of the liver has been possi however, the histology was normal

(5) We have not yet seen such gross changes in th liver-function tests in typical primary myxœdem although lesser degrees of change have been observed.

(6) We are impressed by the steady diminution the size of the thyroid gland during treatment by dr thyroid, this point is not mentioned in the literatu but it was emphasised by Crile in his Moynihan lec to the Royal College of Surgeons in January, 1954

Department of Pathology,
General Hospital,
West Hartlepool
R T COOKE.

Crumpsall Hospital,
Manchester
R W LUXTO

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[1] Cooke, R. T, Wilder E *Lancet*, 1954, i 984

STAPHYLOCOCCAL INFECTION IN THE NEWBORN

ir,—We fear that others, like ourselves may interpret paper by Dr Forfar and his colleagues (March 19) simply as a clinical and bacteriological study but as a ommendation that all infections in newborn babies in ternity hospitals should be treated with erythromycin feel that such a recommendation would be misguided d we should like to comment upon it The clinicians ongst us made the mistake of adopting just such a icy some years ago and we have lived to see its fortunate long term consequences We have also rnt more about the nature and dangers of staphylo cal infection in the newborn as a result both of close laboration between clinicians and bacteriologists and more critical clinical observations in our hospital during past few years We accordingly reversed our previous licy some time ago, and have as yet had no cause to ret this decision The fact that the antibiotic with ich we were concerned was penicillin not erythromycin does not appear to be relevant since as Forfar d his colleagues admit, there is evidence that sooner later staphylococci become resistant to erythromycin

For us the crucial fact is that the more frequently the phylococci in a particular community are exposed to a ticular antibiotic, the more likely are they to become istant to that antibiotic. If there were any overriding vantages to be gained by using an antibiotic as freely Forfar and his colleagues recommend the inevitable dvantage would have to be accepted But although y state that "Edmunds et al (1955) show that early ognition and early treatment of minor staphylococcal ection in the newborn play an important part in venting serious sepsis" we can find no evidence atever to support this statement in the paper to which y refer[1]

We have not treated any case of skin sepsis when t seen during the past twenty months unless it was extensive pustular rash in a small premature baby, we had other grounds for believing that the baby ill

uring this period 163 cases of skin sepsis have occurred tules and paronychia): 11 were treated from the start use of one of the indications we have mentioned 11 e treated later because the local lesions were extending r a period of forty-eight hours observation and the aining 141 cases (86%) received no treatment of any kind n they remained well and the local lesions were clearing or cleared after forty-eight hours.

uring the same period of twenty months virtually all s of sticky eye developing after the first twenty four rs of life were treated simply by local instillation of 10% hacetamide The cases which developed within the first nty four hours were left untreated unless they failed to lve spontaneously during a period of forty-eight hours ervation because we know as a result of earlier work in this spital[2] that a *Staphylococcus aureus* can be cultured from than 10% of these early cases. Altogether 470 cases of ky eye were recorded during the twenty months.

We should like to mention that no serious infection of y kind (pneumonia, osteitis &c) developed in any of 633 babies suffering from a superficial infection and ated on the conservative lines we have indicated

We did encounter a serious infection during this riod in a baby who died of a staphylococcal pneumonia the thirteenth day of life but there was no clinical perficial infection in this baby at any stage We also d to use a systemic antibiotic on a number of occasions ause a baby appeared to be ill and probably infected the absence of any minor superficial infection whatever We feel that this experience supports our present licy of restricting the use of all antibiotics to an absolute minimum since it has shown that this is not only desirable in theory but also safe in practice The real indication for antibiotic therapy seems to us to be a clinical diagnosis of systemic infection (with or without superficial sepsis) This indication is uncommon, but an effective antibiotic must be used at once in these circumstances and this is an urgent matter on which the baby's life may depend We feel that our chance of being able to use any particular antibiotic with confidence (before *the sensitivity of the organism from the particular case* is known) depends upon our past conduct in relation to that antibiotic. We are very glad to be in a position to keep erythromycin in reserve for the case that really needs it and whose life may very well depend upon it and we would like to think that others were exercising a similar restraint We cannot understand what has prompted Forfar and his colleagues to reverse the much more selective policy which they outlined in 1953[3]

S D M Court
C A Green
J G P Hutchison
G A Neligan

Princess Mary Maternity Hospital
Newcastle upon Tyne

ACID-FAST BACILLI IN ACHALASIA OF THE CARDIA

Sir,—Dr Davies and Dr Roberts (April 23) rightly emphasise the need for critical assessment of the finding of acid fast bacilli in the sputum in cases of achalasia of the cardia with respiratory symptoms A diagnosis of pulmonary tuberculosis may wrongly be made if such organisms are not cultured

Acid fast saprophytes are not uncommon findings in sputa in a number of other chronic pulmonary diseases and it is doubtful if they play any important rôle in them. In the lipoid aspiration pneumonia of achalasia of the cardia however, these organisms may act as pathogens and the bacteriological findings must not be summarily dismissed A fatal infection of this nature and a review of the subject has been published[4] Although mycobacterial strains freshly isolated from such cases generally show an unusual virulence for experimental animals especially mice it is the modification of the host's response brought about by the presence of fat in the pulmonary alveoli coating the organisms that appears chiefly responsible for the resulting illness. The cultural characters of the strains isolated vary from case to case and so these pulmonary infections differ from some of the recently reported non tuberculous mycobacterial skin infections such as that due to *Mycobacterium balnei*[5]

Institute of Pathology
Queen's University of Belfast

James B Gibson

A BARBITURATE ANTAGONIST

Sir —I have read with interest the letter of Dr Morgan McElligott (April 16) in which he reports no change other than a deepening of respirations after the administration of 240 mg of ββ methyl-ethyl glutarimide ('Megimide') to a patient who had taken gr 72 of phenobarbitone Dr McElligott is not quite correct in thinking that the lack of clinical improvement was due only to insufficient dosage Certainly the dose for this case would have been 1 0 g and probably even then the patient would have regressed and required one or two treatments more But the important point is that treatment was not started until *six* days after admission

Megimide appears to be a specific antagonist to barbiturates. At the end of six days there would be little barbiturate in the body By this time however, there would have been extensive cellular damage—e g, cerebral œdema—and one would not expect any drug to reverse this injury

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Edmunds P N Elias-Jones T F, Forfar J O, Balf C L *Brit med J* April 23 1955 p 981
Hutchison, J G P Bowman W D Unpublished data

[3] Forfar J O Balf C L Elias-Jones T F Edmunds P N *Brit med J* 1953 ii 170
[4] Gibson, J B *J Path. Bact* 1953 65 239
[5] Linell F Norden, A *Acta tuberc scand* 1954 suppl no 33

Since we commenced using megimide we have treated fifty cases Two are noteworthy In the first the patient had taken gr 100 of phenobarbitone and treatment was not started until thirty-six hours later This was a difficult case, and ten treatments were given before the patient recovered In the second case gr 114 of quinalbarbitone was consumed, but the patient was treated within three hours An uneventful recovery ensued with one treatment

Department of Pharmacology,
University of Melbourne, Australia F H SHAW

A VISIT TO KOLTUSHI

SIR,—Mr Ruscoe Clarke and Dr Leonard Crome (April 2) write that the objective of study at Koltushi "was an understanding of the functioning of the organism in its unity with the environment" They state that among the "general principles" used at Koltushi one was expressed in the statement "Descartes knew already that environmental factors determine the functioning of the organism by means of reflexes" In their conclusion, they state that they "had no more than a glimpse of the new science" They ask "was it a glimpse into the future?"

We are entitled to ask whether a science based on the study of the "conditioned reflex" is so new Is it a study likely to provide the kind of future we should all desire should come about? In his introduction to *The Use of the Self* by F Matthias Alexander, the late John Dewey wrote in 1932

> "The school of Pavloff has made current the idea of the conditioned reflex Mr Alexander's work extends and corrects the idea It proves that there are certain basic, central organic habits and attitudes which condition every act we perform, every use we make of ourselves This discovery corrects the ordinary conception of the conditioned reflex The latter as usually understood renders an individual a passive puppet to be played upon by external manipulations The discovery of a central control which conditions all other reactions brings the conditioning factor under conscious direction and enables the individual through his own coördinated activities to take possession of his own potentialities It converts the fact of conditioned reflexes from a principle of external enslavement into a means of vital freedom."

Mr Alexander enables a person to provide for his use a self acting as a unity with its environment by the following procedure

> The person inhibits his habitual reaction to a stimulus Thus he allows the head to go forward and up This sets in motion an innate reflex whereby the self as a whole instead of firstly directly reacting to its environment indirectly firstly acts as a whole outwards on the environment in all directions in the greatest possible degree Thereby the integrative action of the central nervous system is given freedom to work at its best Thereby the person is provided with a unified whole self he may use for reacting to his environment with kinæsthetic information about his guidance of his actions working in the best way

Bolton, Lancs MUNGO DOUGLAS

ARGININE DEFICIENCY AND MALIGNANT DISEASE

SIR,—I noticed an abstract of a paper by D L Horrigan[1] reporting the excretion of uracil in 3 out of 5 patients suffering from myeloid leukæmia It occurred to me that there might be a possible connection between this observation and the finding[2] that the growth inhibition of a micro organism by uracil was prevented by arginine It may be that uracil encourages malignant change by suppressing the growth of normal cells rendered arginine deficient by the invading neoplasm, which then grows at their expense The simplest test of this hypothesis would be the administration of arginine in cases of experimental or human cancer

As a microbiologist I am not equipped to make tests, but some of your readers may care to co the possibility

Banstead, Surrey E J MILL

REGISTRARS AND REGISTRARS

SIR,—I am a little surprised to read in your i April 23 so embittered and venomous an epistle as signed by Registrar (W plus) The writer's ignorance military ranks seems equalled by his lack of know of teaching hospitals If by any chance he is likely become a "failed registrar" he may perhaps be ab take shelter under the Strachan umbrella

London, S E 1 J J CONYBEA

SIR,—Registrar (W plus) has raised a subject of interest to all registrars One point which req further stress in the inequality of duties is the fact the same difference in the amount of work done registrars also exists in the teaching, but non profe units

There are many registrars (W plus) working in tea hospitals—not only in peripheral hospitals, as correspondent suggests The group he describes as trars (T) undoubtedly exists in professorial units. T add little or nothing to the every day (and night) ru of a hospital service, but they use the time and faci to acquire further qualifications, and write nume papers On these achievements they are often ele to consultant status in preference to registrars (W with a wealth of practical and useful clinical know and experience

Of course, many of these experimental studies are considerable value, but it is unfair, with the ever inc ing expense of the National Health Service, that expanding number of hospital staff should be seclude this type of work, whilst others of equivalent st provide a 24 hour hospital service Clearly the pr time for writing theses for higher degrees and pub ing articles is when one has sufficient knowledge experience to write with authority on the subject one's choice At the moment many higher degrees obtained by men working in a laboratory on a su chosen and supervised all through by their chiefs, finally examine them Unfortunately in the keen com tion for obtaining a consultant post, higher degre count, but in reality are these higher degrees of an clinical value? I doubt it!

REGISTRAR (W

PROTECTING THE MOTORIST

SIR,—There can be no doubt that in the near fu motorists will be more willing to use safety dev against motor car accidents Crowding on the ro plus a high proportion of fast cars will ensure this

Most car accidents are preceded by a second or of warning During this period the natural reaction behaviour of most passengers can be imagined with description

May I propose the following emergency drill passengers, for consideration by those who h opportunity for experimental examination of the or who have clinical experience of the type of in question? This drill is specifically designed to a injuries to the head and face when passengers are f forwards against the windscreen

The feet are raised and pressed against the d board or against the back of the front seat in the of rear passengers The hands are cupped under t chin, the elbows being wedged in the groins This w prevent whip lash strain of the neck

If this method were to gain medical approval, it m be possible to include it in the Highway Code

Hornchurch, Essex I H J BOURNE

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[1] *J clin Invest* 1954, 33 901
[2] *Nature, Lond* 1950, 166, 1035

MEDIAN-NERVE PALSY AND ACUTE INFECTIONS OF THE HAND

n,—May I add a similar case to those described by Bailey and Mr Bolton Carter in your issue of ch 12? It is one of 42 cases of carpal tunnel syndrome ted during the last four years, upon which a report ow being prepared

butcher aged 49 was seen on July 7 1953 with a pulp ction of the right thumb which had been drained two s previously He had had systemic penicillin for one before incision and for the next two days, and this was tinued He had much pain in the hand and wrist ravated by extension of the fingers, which were held in the tion of rest Movement of the middle and ring fingers greatly restricted the index and little fingers less so thumb could be moved more freely but this caused some n. Pain at rest was in the median nerve distribution l was severe enough to keep him awake There was tender s on the palmar aspect of the hand over the carpus and st joint with diminution of sensation of light touch but pin-prick over the median nerve distribution in the hand. dorsum of the hand was considerably swollen.

For the previous eighteen months he had had pain in right hand with acroparaesthesiae in the distribution of the dian nerve every Friday night which had repeatedly ken him. On Saturday mornings the hand was stiff and mb with limited finger movement and some residual ugh lessening pain this subsided completely by midday Saturday not to recur until the following Friday night. se symptoms had become progressively worse until he had ely been having pain on occasional nights during the week ficient to awaken him (Butchers are busy in South tralia on Fridays, because they have to prepare large ers for the weekend for a population that eats a lot of at and they do not open on Saturdays.)

In spite of continued penicillin and rest in a plaster back with elevation, the hand grew steadily worse the fingers re immobile and their movement more painful, until lly he could have no finger moved passively into extension hout great pain Sensation loss by July 11 was complete ght touch and much impaired to pin prick over the median ve distribution. Tenderness at the wrist was much reased.

Decompression of the median nerve was therefore done July 12 by longitudinal incision through a convenient mar crease The flexor retinaculum was divided fully nerve was found to be swollen and reddened in the ximal half of the carpal tunnel and relatively narrowed dark red in its distal half A little serous fluid was present there was no abnormality of the tendons. The skin was ly sutured and it healed well Convalescence was slow satisfactory He was back at work in four weeks, although ory loss and strength of the hand did not recover fully four months.

On April 18 1955 he said that he has had no trouble since, hand has remained normal, and his working capacity is mpaired The scar is supple pain free and hardly visible

I feel little doubt that the infection caused an inflam tory swelling in the carpal tunnel which converted a odic occupational carpal tunnel syndrome into a ative emergency I think it probable that Mr Bailey d Mr Bolton Carter's cases fall into the same category

In case 1 there was a history of rheumatism in the ds which may well have been a carpal tunnel syndrome d they mention osteo arthritis in the left hand, which in the pes may be a factor in the production of the syndrome case 2 there is no mention of previous history but it is possible that inquiry might reveal that the patient d previous symptoms of median nerve compression Both these patients fall into the age and sex group most commonly ected by carpal tunnel syndrome—i.e., women at or out the time of the menopause Case 1 had been having nptoms for years and these probably first arose at the time the menopause.

In both of these cases the early and marked loss of sensation is particularly interesting As well as the butcher I have en it in one other patient—a man with a severe carpal jury and projection of part of a fractured lunate into the rpal tunnel His flexor retinaculum was divided and the jecting bone removed three weeks after the original injury but by that time he had complete anaesthesia over the median nerve distribution in the hand which took six months to recover There was acute tenderness over the median nerve at the wrist but apart from some loss of finger movement by mechanical interference, there was little motor impairment.

The restriction of finger movement in all these cases must be due to mechanical interference in the carpal tunnel by compression of the tendons. The dominance of sensory loss seems to be a feature of the more acute lesions in the usual and much less acute carpal tunnel syndrome wasting of the thenar eminence and weakness usually come before definite sensory loss Such patients, however often complain of numbness at the finger tips, especially in the early morning which interferes with knitting and sewing

I agree with Mr Bailey and Mr Bolton Carter that the compression in their cases was the result of inflammatory exudate and consequent ischaemia of the median nerve, but I think that there was a pre-existing lesion which narrowed the carpal tunnel, predisposing to the nerve compression This may in some cases be a stenosis comparable to De Quervain's disease or some other factor possibly hormonal but whatever the predisposing factor the median nerve lies in the carpal tunnel in a particularly vulnerable position In none of my cases has any disability resulted from division of the flexor retinaculum This is not surprising in view of the fact that all strong movements of the human hand occur with the wrist in extension The flexor retinaculum in man seems to be a useless structure

I was interested to read that Mr Bailey and Mr Bolton Carter required a longitudinal palmar incision to be sure of adequate exposure and division of the flexor retinaculum I have tried the transverse wrist incision found it inadequate and reverted to the longitudinal. There are objections to this incision, but in practice they all heal rapidly and well with no disability, especially if carefully made in a crease.

As soon as the diagnosis of median neuritis from compression has been established I make it a rule to divide the flexor retinaculum as soon as possible to avoid the chance of irreversible damage to the nerve. The only exception to this rule is in menopausal women with mild symptoms, which may sometimes be completely relieved by œstrogens. But should there be no improvement within a short time the rule still applies

Royal Adelaide Hospital
Adelaide South Australia.

J D SIDEY

IRON DEFICIENCY ANÆMIA IN PREGNANCY

SIR,—The question of iron therapy in pregnancy is a topical one and articles such as that by Dr Gatenby and Dr Lillie in your issue of April 9 are very helpful in dealing with the practical aspects of this subject

May I make one or two comments on points made by them? It is true that there is a high incidence of intolerance to the ordinary ferrous-sulphate tablets but I have hardly ever found intolerance to enteric-coated ferrous sulphate tablets, so it is to this form of therapy I turn when the former fails. The enteric coated tablet costs only about double the ordinary variety Ferrous gluconate, however I am told costs about ten times as much as the simple ferrous-sulphate tablet This may be worth considering It is true that some might argue that there is a danger of the enteric-coated tablet passing through the gut undissolved especially as the ordinary tablet passes a long way (as demonstrated radiologically) However the clinical response appears to be adequate, so I am not unduly disturbed by this

Another point is in connection with parenteral forms of iron therapy, so widely used now Why should an anæmia discovered late in pregnancy be an indication? All the evidence I have seen shows that the response to oral iron should be as quick as to parenteral iron[1] A quicker response, then, cannot be claimed If one ensures that the patient can take, and is taking, her oral iron, by asking her a few days later, then intolerance of oral iron is no argument Finally, I believe that a form of iron-deficiency anæmia which fails to respond to oral iron is very rare indeed Most of these cases will prove to be megaloblastic if a sternal marrow examination is made

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[1] Jennison R. F Ellis H *Lancet* 1954 ii 1245

St James's Hospital
Leeds 9

T F REDMAN

MADE-UP WORDS

SIR,—" Bibliotherapy " indeed ! ! How long are we to tolerate this pompous, humourless, self-important use of long made up words to describe such a simple procedure as providing helpful books for a child or his parent to read ?

Institute of Diseases of the Chest
London, S W 3

J G SCADDING

RADIOLOGY OF PLACENTA PRÆVIA

SIR,—Dr Blair Hartley is doing excellent work in using his special technique for visualising radiologically the calcified placenta in localising its position This, he told us in his letter of last week, he can do in rather less than 1 in 3 cases Just in case there are some, among the many who I hope will read his letter, who have not yet been sufficiently convinced of the undoubted merits of ordinary soft-tissue placentography to take it up, I feel I must reassure them that it is quite unnecessary for calcification to be seen in order to determine the placental position

Dr Blair Hartley says that seeing the calcified placenta is factual evidence, agreed, but it would be a pity if those still hesitating to adopt soft tissue placentography became so disappointed at their failure to *see* the placenta in over two thirds of their cases that they did not finally adopt it and thus denied to themselves and their patients the great advantages of the method

The London Hospital, E 1

ROBERT PERCIVAL

FUNCTIONAL SYMPTOMS IN ORGANIC DISEASE

SIR,—In the final paragraph of Dr Barham Carter's somewhat breezy article last week, there occurs this sentence " The great tragedy, of course, is to miss the organic "

It is surely sad that in 1955 it still needs to be pointed out that this attitude reveals a long out dated overvaluation of the soma, and that the tragedy of missing the psychogenic is neither less nor greater but exactly equal to the tragedy of missing the organic

Thirteen years ago an article appeared in *The Lancet*[2] entitled Neurosis Simulating Organic Disorder This dealt with 50 cases which had been referred by Army doctors to an E M S hospital with a definite diagnosis of organic disease, and in which the condition was ultimately found to be purely psychogenic Any case in which even the suggestion of nervous disorder had been raised was excluded from the series

34 of these patients had been admitted to the medical and surgical wards, and constituted 20% of the hospital intake for the 3 months covered by the investigation,

8 of these patients had spent between them 96 weeks in various hospitals and 106 weeks on light duty,

19 of these patients had between them been radiographed 30 times, including 12 barium meals, 2 barium enemas, and 2 intravenous pyelographies,

7 of these patients had received physiotherapy totalling 35 weeks' inpatient and 56 weeks' outpatient treatment

All this staggering waste of professional time and public money was not merely useless to these patients, but actively harmful to them in that it confirmed original fears that they had some serious organic di In many cases it probably made them ther inaccessible to psychotherapy and condemned to a of invalidism

I suggest that this also is a tragic issue I that while both these types of medical error are " the great tragedy " lies in the lack of that bal psychosomatic approach which would make a do is ashamed of missing a psychogenic disorder as he is of missing an organic one

London W 1

ALAN MCGL

MASKED EPILEPSY

SIR,—I have closely followed the arguments in rel to Dr Wallis's paper of Jan 8 If one agrees that in the leg, cyclical vomiting, headaches, pyrexia, abdominal pain are fairly common manifestation epilepsy, how far does this help in the treatment ? these cases the forerunners of Halhuber's auton dystonias,[1] or the "*Manager-Krankheiten*" of the generation ?

I agree with Dr O'Neill (April 2) and his tension th These cases need more than phenobarbitone Bu exploration of the child's mental state and his env ment must take too long and there are too few psy therapists I look forward to controlled research hypnotherapy Tension appears to be rapidly destro and the child is defended against himself As Bram says[2] " He becomes more in control of his organism

London, W 1

GORDON AMBRO

SANATORIA

SIR,—I read Dr Edwards's letter last week interest While agreeing to a large extent with wh says, I think there is one factor he has not mention namely, that it is quite possible that in the near f patients will refuse to go to sanatoria many miles d from their homes

As regards teaching tuberculous patients " to with their disease," I would say that diabetic pa learn to live with their disease very satisfactorily wi having to go to special institutions for the pu Nevertheless, I quite agree that there is still a place sanatoria in the treatment of tuberculosis, provided are near the centres of population that they serve.

Hastings

A W ANDERS

THE DIFFICULT APPENDIX

SIR,—Every young general practitioner should the article by Mr Kerr in your issue of April 9, reveals the many difficulties in such a common diso and older readers may be consoled over their failures, either in not operating soon enough or in rem ing a normal appendix Two of my own cases may th some light on our difficulties

One hot summer a 7 year old boy suffered from indi and diarrhœa He was still playing with his friends b he had no fever, pain, or vomiting, till sent home by a mother because he was incontinent of liquid fæces He put to bed by his doctor, who was told about generous of unripe apples Bismuth was prescribed Three days though not complaining of any pain, he was admitted to pital suspected of salmonella infection (leucopenia splenomegaly, and diarrhœa) In a couple of days he to improve He had neither fever nor pain, but a leucocy developed A surgeon concluded that there was no su cause, and that the condition was probably paraty That night the boy collapsed with upper abdominal pain rigidity, black vomit, and meteorism A perforation suspected and the abdomen was opened, but a gangre

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[1] *Lancet*, April 23, 1955, p 868

[2] Cook, G T, Sargant, W *Ibid* 1942, i, 31

[1] Halhuber, M. J *Ars Medici, Liesthal*, 1953, 43, 182

[2] Bramwell, J M Hypnotism. London, 1930

l appendix and an abdomen full of pus was found
died three hours later
ar-old girl complained of colic and vomiting Her
ure was slightly elevated No typical muscular
could be found in the abdomen but by palpating
the cæcal region some resistance was noted The
was removed but it was only slightly red No
cal examination was made. Her general condition
ted with continuous vomiting meteorism, and
When I first saw her the child was seriously ill with
nose acetonuria, and leucocytosis (23 000 per c.mm
ft to the left and toxic granulations) X-ray examina
the chest showed that the diaphragm was high
ed poorly but there was no other abnormality An
ous drip of glucose-saline solution followed by plasma
time for arguments to be considered in favour of
ng the abdomen Within two hours the child underwent
llous change: no vomiting no fever less meteorism.
w was that this was a case of cyclic vomiting with
mia. Within a week the child was discharged
ly fit

D P R KEIZER.

mm.

POLIOMYELITIS VACCINES

—The Salk anti poliomyelitis vaccine is prepared
monkey tissue cultures Is it certain that injection
s preparation will not produce rhesus antibodies
injected into susceptible human subjects, most
ially those already sensitised?

tminster School of Medicine
London, S W 1

J G HUMBLE

RUPTURE OF LAPAROTOMY WOUNDS

,—In reading Mr Standeven's article of March 12
the subsequent correspondence I have been struck
he lack of reference to what I believe to be a most
rtant feature I have re sutured over 30 burst
mens and in all cases I have noticed the firm
rence of part of the prolapsed bowel or omentum
he edges of the peritoneum and the subcutaneous
es. Surely this suggests that some part of the peri
um has given way at an early stage Small gut or
ntum protrudes and lies just deep to the skin
toneal fluid escapes and (I believe) delays healing
the superficial layers When the skin stitches are
ved the whole wound disrupts and more bowel may
h prolapse

r Standeven and Mr Walsh (March 26) rightly
s the significance of the serous discharge In my
rience this always indicates an impending rupture
uch cases inspection and percussion may demonstrate
t small bowel lies just below the skin

believe that the most important layer of the
ominal wall is the peritoneum Unfortunately it is the
akest If the patient is straining at the time of its
ure the peritoneum may split at right angles to
line of suture In several cases I have found the
ure line to be intact but bowel escaping just lateral
it

doubt if the incidence of dehiscence of laparotomy
unds is in any way influenced by such general factors
anæmia or protein or vitamin deficiency—or even
al sepsis. If the peritoneum stays intact there will
no burst abdomen I feel therefore that Mr
ndeven's distinction between early and late ruptures
an artificial one If the skin stitches are left in till
te the skin edges will probably hold The later a
rst abdomen occurs the more difficult it is to separate
rt of the bowel from the subcutaneous tissues

In my own experience I have found that:

(1) Transverse or oblique incisions are less likely to rupture
an vertical ones because the pull of the abdominal muscles
es not tend to separate the peritoneal edges

(2) The abdominal wall must be relaxed until peritoneal
suture is complete

(3) Nylon is unreliable

(4) Short ends of knots must be left long and the gap between stitches kept short

(5) The peritoneum is less likely to split if a horizontal mattress suture is used

A J WALTON

The London Hospital, E 1

SIR,—Like other correspondents, I found catgut and monofilament nylon unsafe in suturing the rectus sheath Interrupted thread and silk was secure but tedious to insert For three years now I have been using continuous braided nylon (Finlayson's no 6 green) It is pleasant to use and so far safe Although there have been some infected wounds it has only once been necessary to remove the suture

Braided nylon has more elasticity than monofilament nylon so should be less likely to cause the tight feeling in the wound mentioned by Mr Oldham (April 16) This sensation has been mentioned by only one patient but has not been asked for specifically so may well be more common Certainly the knots are unobtrusive

A. M DICKINS

London W 1

HYPOGLYCÆMIC EFFECT OF DIMERCAPROL

SIR,—Concerning the preliminary communication by Dr Butterfield in your issue of March 5 the papers on sulphur and diabetes mellitus published by Prof Andreu Urra and myself from the medical clinic of the University of Seville are perhaps unknown in Britain These papers were based on a series of experiments which are the subject of my thesis on the problems of sulphur and uric acid in diabetes mellitus[1] Professor Urra and I have also published another paper on sulphur and the metabolism of glucosides in diabetes mellitus.[2] In these investigations, low levels of glutathione were usually found in diabetic blood and experimentally alloxan diabetes was prevented by giving preparations of sulphur We treated diabetics with dimercaprol and found only a slight tendency to reinforce the action of insulin and hyperglycæmia and glycosuria improved

MIGUEL RIOS MOZO

Seville

BURNS FROM ELECTRIC BLANKETS

Mr F Grisley B.SC managing director of the Warm Glow Co Ltd, writes:

In your issue of April 2 Dr Neville Davis reports an accident with an electric blanket To avoid risk of accidents the manufacturers normally instruct the user to switch off the blanket before getting into bed but people often disregard this advice Alternatively a waterproof sheet may be used between the blanket and the sleeper This also may be disregarded, or a worn or pervious sheet used with disastrous results. The use of an earth as suggested by Dr Davis, is impracticable and even dangerous for the blanket should be an earth free appliance with no exposed metal parts.

In 1948 my company introduced a plastic-covered waterproof element into all our blankets. This not only prevents danger from bed wetting, but it also enables the whole blanket to be immersed for laundering The plastic covering used is stable and flexible, and lasts indefinitely This particular kind of accident therefore need never occur

PLASTIC APPLIANCES MOULDED DIRECT TO PATIENT

Mr R A E. Walker secretary of the National Research Development Corporation writes

In his article of April 23 Dr Brennan refers in a footnote to patent application no 10609/51 It may not be clear to your readers that this application relates to the proposals communicated to us by Dr J T Scales of the Institute of Orthopædics Royal National Orthopædic Hospital Stanmore for the preparation of composite material of 'Polythene (polyethylene) and Moltopren (polyurethane) and the moulding of surgical splints therefrom by application to plaster casts or directly to the patient The patent rights in Dr Scales's invention have been assigned to the Corporation for exploitation in accordance with the Development of Inventions Act 1948 Application may be made to the Corporation for further particulars.

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[1] *Hisp Med* (in the press)

[2] *Folia Clin Internal* May 1953 no 5

Obituary

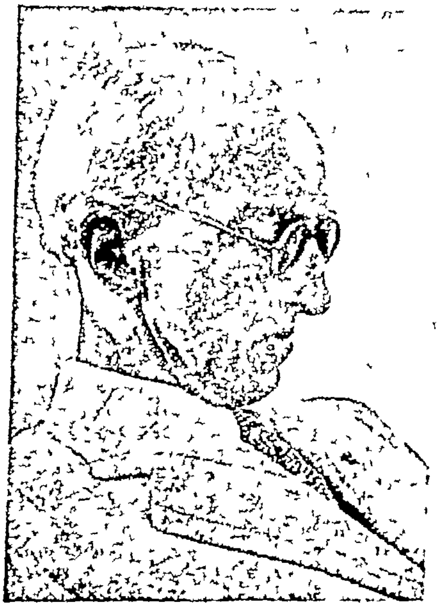
EGBERT COLEBY MORLAND

M B, B Sc. Lond, M D. Berne, F R C P, F R C S
EDITOR OF THE LANCET, 1937-44

In the development of a journal a few men and women play outstanding parts The influence of Dr Morland's original mind and new points of view was apparent from the time he joined the staff of *The Lancet* in 1915, and it continues through those he taught

In few ways an ordinary man, he brought to his main task a knowledge and experience as unusual as it was useful

He was born on Sept 3, 1874, the fifth son of Charles Coleby Morland, J P, of Croydon, and his wife Jane Fryer The Morlands and the Fryers were Quakers from the North of England, and the Croydon family was both brilliant and unconventional Egbert, a clever but uneasy boy, was sent to the Whitgift Grammar School and then to Bootham, the Friends' school at York. A taste for science was confirmed by a period at Owens College, which also gave him a lifelong bond with Manchester He took his B SC with first-class honours in zoology, and went on to St Bartholomew's Hospital with a senior scholarship At Barts he won the Matthews Duncan prize and was vice-president of the Abernethian Society, and after taking the London M B in 1898, with the gold medal in physiology and honours in anatomy and organic chemistry, he became successively ophthalmic house-surgeon and house physician at his own hospital, and house-physician at Wolverhampton General Hospital His next appointment, in 1901, was at Great Ormond Street, and it was then that the natural sequence of his career was rudely broken He developed tuberculosis



Like many another medical victim of this disease, he presently found himself making it his special study The first fruit of this new interest was an essay on the design of sanatoria, entered for an international competition held in 1902 before the King Edward VII Sanatorium was built at Midhurst There were 180 competitors, and with the aid of his architect brother Morland gained third prize for his plans, which were published in the first issue of *The Lancet* for 1903 The new phase in his life was soon established, for after living for a while in Switzerland to recover his health he decided to remain and make his home in the mountains In 1903 he married Mary Windsor Latchmore, a woman of zest and character who helped him devotedly till her death in 1948, and when he had taken the Swiss Federal Diploma they settled at Arosa, where he practised in three languages and from 1907 to 1914 directed the Villa Gentiana, an English sanatorium In 1905 he was writing in these columns, with W R Huggard, on the action of yeast in tuberculosis and its influence on the opsonic index, and his M D thesis at Berne in 1907 was on opsonins—a subject then in the bacteriological forefront From the German he translated Turban's *Diagnosis of Tuberculosis of the Lung* and Bandelier and Roepke's *Tuberculosis in Diagnosis and Treatment* In 1913 he produced a small book, written with Clive Rivière, on *Tuberculin Treatment*, and a paper on technique of artificial pneumothorax

This phase was ended by the outbreak of war, and next began almost by chance Now some 40 years he left Switzerland to join in the Society of Fr relief work on the Marne Before doing so, however, had displayed his journalistic talent by abstracting *The Lancet* a statement by Paul Eltzbacher on food supply of the German people, and when twenty-column contribution arrived one day ju the journal was going to press, the editor had paid compliment of holding back the week's issue until it be included When Morland returned to London the Marne and called at the old *Lancet* office at the co of Bedford Street and the Strand, Sprigge wa difficulties because Gerald Horner, then assistant ed was serving in the R.A M C, so he said to Mor "why not stay and help?" And Morland sta for 29 years

At this point one might follow the precedent of Hebrew biographer who referring his readers to the b of the Chronicles of the King Israel and Judah But though bound volumes of *The La* since 1915 contain most of acts of Morland, and would h been very different without h what he did himself is inextrica mingled with what other peo did In an effort to analyse influence it has been truly that he found the journal hum but left it human, but perh his greatest effect on our colu was one of refreshment He this effect because he was artist and (to the end of unexpectedly long life) a petually surprising person

The artist enables people to familiar things anew, and land had just this faculty angle of vision always seemed be a little different, and, th this often embarrassed and so times alienated his acquaintan it helped him to be not only an animating journa but an exceptionally valuable member of our profess for to look at things at a new angle is often hig instructive He also had the catholic curiosity of investigator and was ready to be thrilled by any fr thought or fact—though he might lose interest quickly When he wanted to do so, he could absorb body of knowledge very thoroughly, and he rememb a great deal about a great many diverse subjects, fr mathematics to midwives, from infant feeding to European flora, but he had little intellectual taste generalisation, and tended to look at one thing at a ti "on its merits" Hence, as an artist, he preferred t small canvas to the large one, and he enjoyed paint detail But whether the canvas was large or small, would avoid monotony by an engaging touch inconsequence in the composition

If this is not the portrait of a creative thinker, it nevertheless the portrait of a born journalist, born make others think Moreover, in this delicate and of exhausted man—the "old poitrinaire" as he call himself—the mental liveliness was matched and ma profitable by an astonishing capacity for work, day day out, year in year out Skimming, as it seem through the millions of words that poured into th office, he could quickly detect what was new and intere

Morland, when he wanted, could write so catalytic a letter as to draw a contribution from the most unreactive of experts, and even his routine communications were carefully written in a personal way—often in fact by hand But it cannot be said that even through the post he wholly satisfied everybody , for ordinary people often prefer ordinary letters, and few besides harassed editors know how correspondence may improve if allowed to " mature " Those who went to *The Lancet* oracle with a question must be prepared for an oracular reply, which left the " onus " (to use another of Morland's favourite words) on the person receiving it The following, for example, is his answer to a long letter from a doctor who wanted to know about the copyright regulations governing the reproduction of *Lancet* material in foreign broadcasts

Dear L ,

I am glad to hear you are helping the British Council to let South Americans know what British medicine is doing We do our own bit too I don't feel I can give you any general guidance on copyright in the air But you would find the Golden Rule applicable and between ourselves the Hippocratic Oath is binding

With kind regards, Sincerely Yours,

EGBERT MORLAND

Copyright was one of the subjects that did not interest him

Even his colleagues seldom had their questions answered directly or comprehensively But when his mental processes seemed to be at their most devious and detached the probable reason was that he was not yet ready with his decision, which he would give in his own time and his own way It was partly because he was so puzzling that he was so fine a teacher , and, whether amusing or infuriating, his enigmatic instructions somehow extracted from his juniors the same kind of effort that he himself put into *The Lancet*

Nor did this taste for the oracular prevent his being energetically practical in other fields when something within his compass needed to be done Hence in his spare time (which did not exist) he did solid work in many useful causes , and in various ways he was of service to the Queen Alexandra Sanatorium at Davos, to the Enham (now Enham Alamein) Village Centre for Disabled Ex Servicemen, to the Medical Defence Union, to the Society for the Relief of Widows and Orphans of Medical Men, and to Sibford School, of which he was a governor But, though a good speaker, he seldom appeared on platforms or at the meetings or dinners of medical societies Disliking public occasions, he was inclined to think that an editor should be a back-room boy, neither seen nor heard except through his journal, and invisible especially to callers None the less he was a sociable person, and never more happy perhaps than in the Athenaeum, which likes a proportion of its members to have their eccentricities He was happy, too, in the fellowships conferred on him by the Royal College of Surgeons in 1936 and the Royal College of Physicians in 1941 , though both colleges probably wanted to withdraw their honours when they saw that he described himself (whether to save space or out of modesty) as FRCP&S

When Morland succeeded to the editorship in 1937 he was already 62 , and two years later, when war broke out and the decision was reached to move the journal out of London, he was tempted to resign his sisyphean task But, as it turned out, the move to Aylesbury proved a tonic Settled cosily in a flat above the tiny office in Temple Street, he abandoned even the convention of office hours and did most of his downstairs work after supper when his juniors had gone home Freed from the social obligations of his chair, and disguised from former friends by a beard and a dilapidated mackintosh, he took an eager interest in the war-time life of the small market town, and spent more of his time in reflection and reading—though even now he never finished a b preferring the random sample With a senior's less of inhibitions, he was finding it easier to show abundant kindness of heart and concern for oth but to keep the balance he showed also more of sharpness of his tongue When directed towards rather than individuals, this asperity was gene enjoyed, and it is pleasant to find in our files his de comment on a rather pompous declaration in distinguished signatories defended the rights and l of the citizen Underneath, in his small, neat, decor hand, Morland has written

I'd rather be in prison with my friends th free with that lot. Ed. L.

It was sad, in a way, that he should not take comm of his journal until his most active years were p for he never got full credit for his achievements, these were different from what they might otherwise h been But possibly *The Lancet* did not lose ther for in his more impetuous moments he often nee someone to tell him to think again Moreover, tho he could rule both by love and by fear, he was not a b commander he was a prophet or priest rather th king—an impish prophet but in direct line from the Testament During the war he was already an old with the defects of his high qualities becoming apparent, and it was inevitable that in his cour Aylesbury the executive responsibility should dev more and more on his lieutenants—as once it devolved from Sprigge to him So the honour burden was partly transferred to younger shoulders, when *The Lancet* returned in 1944 to London Mo retired into private life—with a characteristic valedic greeting to his readers

At first at Aylesbury, and afterwards in an old s house beside the ancient Friends' meeting hous Wooldale in Yorkshire, he adjusted himself yet aga new circumstances He had given much thought to age—its disabilities and possibilities—and had m been one of the first to see the need for a conc movement for old people's welfare, comparable complementary to the movement for infant welfare w developed during and after the previous world war 1945 he expressed his ideas in a charmingly Morla pamphlet called *Putting Them on the Map,* written f Buckinghamshire committee of which he was instiga member " We must search out the old people in t hidey-holes," he said, " and find for ourselves whe they are content with their lot, whether it is a lot which they should be content, and if not what we sh do to amend it " Himself, he well understood the v of continuing to be active, and as lately as 1951 he w the biography of a pioneer midwife, entitled *Alice and Stork* He had the advantage of being one of those wh pleasures are of the mind, and for some years of retirement he was also fortunate in his keen enjoym of gardening and walking, and in the companionship his wife But each in turn was taken from him, eventually almost all the power of sight By refinement of age, and its distresses, his face bec less that of a prophet than a saint—a rôle to which had never aspired One of his chief hopes, he said that he might continue to amuse those around him.

He died at York on April 26, in his 81st year even to the last his mind, though wayward, reta the ardent quality that so often made him seem youngest, though maybe also the oldest, of his comp Throughout his life he belonged to the present and future rather than the past , and many who knew h as well as many who did not, have cause to be grat for his disturbing, enlivening, and enlightening spirit

WILLIAM BURRIDGE

D.M. Oxfd

Dr William Burridge formerly professor of physiology d principal of the King George's Medical College and n of the faculty of medicine at Lucknow University d in hospital at Dartford, Kent, on April 21, at the of 69 He was the author of *Excitability a Cardiac dy* (1932) *A New Physiology of Sensation* (1932) *New Physiological Psychology* (1933) and many short les in various journals.

A T B writes 'Like his fellow Cornishman mphry Davy, and his pupil Faraday Dr Burridge de important discoveries through brilliantly original periments using very cheap and simple apparatus s book *Excitability* describing his experiments on frog's heart is a medical classic, and this study the beating heart's responses to stimulation enabled n to correlate similarities in nervous action and con ous sensation to deduce rhythmical activity in brain d spinal cord neurones and in sensory end-organs and elaborate many logical consequences of assuming ythm in neurones. The fact of rhythm in cerebral urones has since been independently confirmed by er workers some of his predictions remain to be oved by experiment.

"So far Dr Burridge's work has not received the eral acclaim it deserves. We owe to him the new d revolutionary concept of responsiveness as distinct m excitability, a new method of research in pharma logy, giving new and surprising information on the ltiple actions of some drugs and their quite different ects in large and small doses and a new physiological chology harmonising experiment, sensuous experience d deductive reason and well in advance of any previous ory of sensation and of thinking process.

His own explanation of the opposition that his work d theories met was the power of an orthodox primary umption to blind fully organised minds to any new th that contradicted teaching elaborated from the mary falsely generalised preconception His Puck ing the Doctors (*Medicus* December 1952) gives a l statement of his defence and repays reading

PATRICK KERR DIXON

M.D Dubl. F.R.C.S.I

Dr Patrick Dixon who died on April 21 at Lusaka rthern Rhodesia, had spent nearly thirty strenuous and venturous years as a medical missionary in the Belgian go.

He was born in 1898, the son of the late Andrew on, professor of anatomy and dean of the school of ic at Trinity College Dublin Patrick's studies Trinity College were interrupted by the 1914–18 r and he was mentioned in despatches for services th the Royal Garrison Artillery in France In 1918 returned to Dublin to graduate in 1922 in science, h first-class honours in mathematics and experimental ence. Two years later he graduated M.B with honours. In 1926 he joined the Garenganze Evangelical Mission the Belgian Congo

For the next twenty five years, despite the effects of re injuries sustained when he was mauled by a lion, he rved the people of the Luapula Valley with devotion the course of his work he saw the suffering caused by choma and in 1920 he visited India to study this ease under Sir Henry Holland His published work ls with his experience of its treatment in Central Africa. e hospital which he founded at Chibambo became a ntre for the treatment of eye diseases. In recognition of services he was decorated by the King of the Belgians. In 1932 ill health forced him to leave the Luapula alley, and for a time he was medical officer at Nkana ine In 1933 he joined the staff of the Government frican Hospital at Lusaka He also taught at the frican Medical School

A colleague writes: 'Pat Dixon was an eager tireless d devoted worker, content to make do with the most eagre equipment yet keeping himself up to date in the edical world and always looking forward In this he as a true disciple of the great Dr Livingstone who had amed the same country fifty years before Like him o, Dixon bore to his dying day the marks of the lion's unch in his left humerus. He will long be remembered on the divide between Congo and the Zambezi watersheds'

His first wife, Miss Olive Arthur died in 1927 In 1934 he married Miss I H Russell who survives him with a daughter of his second marriage

KENNETH BENSON BELLWOOD

O.B.E., B.A, M.B Camb., F.R.C.S.

Dr Bellwood consultant surgeon to the ear nose and throat department of Bedford General Hospital, died at his home on April 17 at the age of 64

He was born in Middlesbrough and was educated at Coatham School, Redcar He was a scholar of Pembroke College, Cambridge, where he took the natural sciences tripos in 1912 and a Shuter scholar at St. Bartholomew's Hospital qualifying in 1914 During the 1914–18 war he was appointed O.B.E. for outstanding service in the Royal Navy In 1917 he took his M.B Soon after he returned to civilian work he entered general practice in partnership with the late W H Miller in Bedford and also specialised in diseases of the ear, nose, and throat. In 1921 he obtained the F.R.C.S. When in 1930 he was appointed E.N.T surgeon to the Bedford County Hospital he laid the foundation of the present successful large and busy E.N.T department at the Bedford General Hospital Despite ill health which first showed itself in 1940, he worked indefatigably, and he was appointed consultant surgeon to the department when the hospital was taken over by the National Health Service in 1948

G A M writes: 'Dr Bellwood, as he is called by all in Bedford was loved for his quiet modesty and great kindness to all his patients The greatest sorrow will be felt by the patients he looked after as a general practitioner He loved the hills, and was a great walker in his day Even when he could no longer climb he always went north to his beloved Yorkshire for his holidays'

In 1921 Dr Bellwood married Florence Violet Cooper, who survives him with two daughters

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Appointments

BELCHER J. R. M.S. Lond., F.R.C.S. M.R.C.P: asst. thoracic surgeon *Middlesex Hospital London*

DAWES J D K M.D Durh F.R.C.S. asst consultant surgeon E.N.T department Royal Victoria Infirmary Newcastle upon Tyne and surgeon to the Newcastle upon Tyne R.H.B

GRIFFITHS E. P M.R.C.S D.OBST D.C.H asst M.O.H., Gloucestershire

MATHER, J F M.B Durh.: school M.O Newcastle upon Tyne

MILLS, W G, M.B. Birm F.R.C.S., M.R.C.O.G part time consultant obstetrician and gynæcologist mid Worcestershire group Birmingham R.H.B.

SKONE, J F M.D Lond., D.C.H D.P.H D.I.H M.O.H., chief welfare officer and principal school M.O West Bromwich.

South-Western Regional Hospital Board:

LEAHY T C, M.B. N.U.I S.H.M.O Hortham Brentry hospital group Bristol.

WALKER, W I M.B Aberd D.P.H., D.P.M medical superintendent, Hortham Brentry hospital group

WALLEY R V, M.B. Camb deputy resident physician Ham Green Hospital near Bristol

Manchester Regional Hospital Board:

HOYLE THELMA B, M.B. Manc., D.A asst anæsthetist (S.H.M.O.) Burnley and district hospitals

KIRBY J H. M.B Leeds D.M.R.D consultant radiologist Wigan and Leigh hospitals

O'REGAN JOHN M.B. N.U.I., D.P.H tuberculosis physician (S.H.M.O.) Preston and Chorley hospitals

Liverpool Regional Hospital Board:

JONES C H., M.B. L'pool: whole-time asst. pathologist Alder Hey Children's Hospital Liverpool.

RICHARDSON J G M.B. L'pool F.F.A R.C.S. D.A consultant anæsthetist Liverpool city area.

WALKER G D D.M Oxfd M.R.C.P consultant physician superintendent Newsham General Hospital Liverpool

WALLACE JONES D R M.B. L'pool D.M.R.D consultant radiologist North Liverpool and Fazakerley groups

The Hospital for Sick Children, *Great Ormond Street, London:*

BAILLIE R C M.B. Lond house-surgeon orthopædic and plastic departments

JOHNSTON W H M.D Toronto: asst medical registrar

SMITH, ISABEL G M.B Lond., D.C.H house physician

TODD J J M.D Toronto F.R.C.S D.C.H: part time surgical registrar

WYLLIE, G G M.B Adelaide F.R.C.S.: resident asst surgeon

East Anglian Regional Hospital Board:

COLLINS F M M.B Lond M.R.A.C.P: physician-superintendent Papworth Hospital

GILLIE, ALEXANDER, M.B Glasg asst psychiatrist Little Plumstead mental-deficiency group of hospitals and child psychiatry service

MARTIN W M M.B. anæsthetic registrar Newmarket General Hospital

WELLS J M WESTON, M.R.C.S. D.M.R.D consultant radiologist King's Lynn and Wisbech area

Notes and News

HEALTH EDUCATION

AT the seminar for public health workers organised by the Central Council for Health Education of Great Britain and held in London from April 19 to 23, delegates attended from 21 countries Dr W Emrys Davies, education officer to the council, said that people do not listen to instruction unless they feel that the subject matter is relevant to their own problems and way of life Hence the first task of the health educator is to assess the basic human needs common to all, in any country, whatever the conditions or climate The second is to establish an atmosphere in which discussion can flourish, and experiments have shown that the discussion group can achieve what its members could not achieve singly The group leader is therefore a more effective person than the lecturer talking to an audience and isolated from his hearers by natural barriers of platform position, shyness, and absence of communication of ideas between members of the audience Dr John Burton, medical director of the council, described the use of case histories which command interest from members of a group and which recall to many experiences that can be used as a basis for discussion Mr W Sellers, film advisor to the Colonial Office, said that in dealing with illiterate people one must evolve three dimensional visual aids which come within the range of their everyday experience Diseases have to be classified in relation to their causes and source—e g, insect infections, airborne and water borne diseases In Nigeria a film van has proved a big attraction because people will comprehend a moving picture when the still one makes no impression

UNDERGRADUATE TEACHING IN LONDON

THE difficulties of undergraduate teaching hospitals arising from the shift of population from the centre of London are mentioned by Colonel J J Astor, chairman of the board of governors of the Middlesex Hospital, in the hospital's statistical report for 1954 At the Middlesex the bed occupancy rate is over 90%, and the pressure on the outpatient department is as great as ever, but " there is a tendency for clinics and wards to be deprived of various types of case which are valuable for undergraduate teaching Patients suffering from these conditions are now for the most part being treated at hospitals in the peripheral areas, and in consequence medical students of today are not seeing the cross section of illnesses which was available for their predecessors when this was still a residential area " As an interim measure the Middlesex has arranged with the Luton and Dunstable Hospital for some of the patients on that hospital's waiting list, with their consent, to be transferred to the Middlesex for treatment, and this scheme is working well

"THREE MEN" [1]

Miss Jean Evans, a writer who has turned her talent to presenting the case histories of three living men, describes her book in a sub title as "an experiment in the biography of emotion" Johnny Rocco began life as a rejected child who was often delinquent, but who has finally made a precarious social adjustment William Miller, too, was often delinquent till he became blind, he recovered his sight but (perhaps finding the responsibilities of sight too heavy) became delinquent—and blind—again Martin Beardson is a tormented homosexual She tells their stories with sympathetic insight, but without interpreting the psychological mechanisms at work. It was inevitable that she should select, from the vast quantity of material she has amassed in the course of her long and friendly association with these men, which facts and which letters and conversations to report, but she has a biographer's skill in choosing what is relevant, and the reader is confidently aware that the picture is true, distorted neither by compassion nor censure Prof G W Allport, professor of psychology in Harvard University, notes in an introduction how valuable he has found the book in the teaching of students Because Miss Evans has avoided imposing her own interpretations, students are stirred to ask questions, and hence to discover much about some common forms of mental sickness. "The first requirement in good teaching," as Professor Allport says, "is to excite greedy curiosity" These cases, he finds, do exactly that

University of Liverpool

At a recent examination for the diploma in tropical med and hygiene the following were successful

P B Acharya, A A Akiwumi, S H Bokhari E J M A Jafri Prakong Kecharanantana N H Khan T J Ma J I Maxwell, H Medina P A Y Narayanan Margaret C Bridget O'Keeffe, A V Rao, J B Roy, G Singh, S

Dr J B Roy has been awarded the Milne medal in medicine, and Dr J I Maxwell the Warrington Yorke in tropical hygiene

Royal College of Physicians of London

At a comitia held on April 28, with Sir Russell Brain, president, in the chair, the following were elected to fellowship

J F LANDRETH Christchurch New Zealand, J L Fra London J H HALLIDAY, Sydney, R I MACDONALD, To F E PILKINGTON, South Brent, Devon, R L WATE London, A C STEVENSON, Belfast, H A TREBLE, Cante J C RICHARDSON Toronto, J F LOUTIT, Harwell, T E Newcastle upon Tyne, R B KERR, Vancouver, R N TATTE Leeds, A C DORNHORST London, W S SUTTON Liver B G PARSONS SMITH, London, F H SCADDING, London, LEIGH London, H V MORGAN Khartoum, L D W S Glasgow, D A WILLIAMS, Cardiff, C F HAWKINS Birmin R D TONKIN, London H P WILLIAMS Coventry, A WILLIAMS Kampala, J R ELLIS London R A JONES Cambs, E K CRUICKSHANK, St. Andrew, Jamaica, MACDONALD, London B G MAEGRAITH, Liverpool, W A KARUNARATNE, Colombo

The following were elected to the fellowship under by 39b, which provides for the election of non members " have distinguished themselves in any branch of the sc or practice of medicine "

I DE B DALY F R S, Cambridge, K G V NYLIN, Stock W G PENFIELD, O M, F R S, Montreal, G F STRONG Vanco

The following, having satisfied the censors' board, elected to the membership

J H Allison, M B Lond squadron leader R.A.F J B B M B Witwatersrand, G P Blanshard, M D Camb, C R Bo M B Sydney J A S Brine M.B Melb F I Caird B.M A. S Cooper M B Camb, J E Cosnett, M.D Witwater A J P Crowden, M B Lond, J A Davis M B Lond J B D B.M Oxfd F E Dreifuss, M B N.Z. M de L F M.B Adelaide Judith M Fitzsimons, M.B Camb Peter F M B N Z, A D Forrest M.B St And, T C Gibson M.B. M P W Godfrey, M.B Lond, K L Granville-Gros M B Lond, Robert Hecker M.B Adelaide Anthony H M B Edin. Bernard Lennox M D Durh. G D Lumb, M.D J B McFadden, M.B Sydney D C Morrell M B Lond, lieutenant R A F A E Mourant D M Oxfd C G H N M B Lond L J Pinto M D Bombay D E B Powell M.B. surgeon lieutenant, R.N V R., F L Richardson M B Birm, R Rischbieth M B Adelaide, Daniel Rooney, M.B Belf, J A R L R C.P, P D Saville, M.D Lond, Eric Schiller, M.B S D J Sheehan, M D Lond, wing commander, R.A.F W D M B Glasg Eileen M. Spence M B Aberd V H Springett Lond, Bernard Tabatznik, M B Witwatersrand E J W Williams, M B Camb, Wickrama Wijenaike, M B Ceylon

Licences to practise were conferred upon the fol 125 candidates who have passed the final examination of conjoint board

Nazir Ahmed B G Andrews, Martine Y K Armstrong M Aylott, B J Bartley, Esther A Bence, A E Blumenfeld I Bowen T A Boxall, G E Brennan, D E Brooke D J Br J D Broome E H Burgess, Brenda J Butcher P R Br P H Byles H C I Bywater, D A O Cairns J J Camp, Gil Cann, Elizabeth A Capell J A Chappel, Mary D Clarke, B Clayton Payne, Terry Coates J A B Crawford, E A P Cro D E Dart, H T Davies, K S Davies, D T F Deakin E Dingley, Patricia A Dinkel, Elaine C Donoghue Denise J Duc Sheila M. Eades P M. Elwin Verna P Firth, J D W F C B Floyd B H Foakes C B Franklin A G Giddins, D Gooding, B G H Grant, H C Grocott Beryl M. L Hall P Hamber C N Haynes, Rita Henryk Gutt, Molly Hill, P Holt Judith C Howard, P J C Howe, J G J Howell Elizabeth Hudson, Rosalinde Hurley, R H Huzzey, D E Hyams, Caroline Jones N L Jones N H Kemp, D A Kennard A G Yuin B Ling Evelyn C Lock J A London, B H McC B B MacGillivray T A R. Mahmoud Barbara L. Mar Royston Mason, J S B Meyer Marion V Miles, J D M S F W Monkman W P N Moore, J G Morris, A. I M M W N Nicholls W B Obank, F A Orhewere, Dolly I Pak Giuseppe Pampiglione J G Parkes, G W. Peacock, G D Pe G B Phillips, T A Plumley G G Pollock, C A Poulter, C A Procope M J Prophet, Elisabeth J Rashid Victor Ratner, Ami Reed, G R E Roberts, J T Roberts Bruce Robertson, D Rothman, Theodore Rowan, N E Rust, M. L Rutter, D Saunders G W Scott Joanna Sheldon, B S Smith David S Barbara Y Stockhausen J M. Stratton Rhona Stringer M Swann D M. Symes Lionel Tenby, Ping Kun Teng D E Thomas T J Tiplady P J Toghill Chai Hee Tsao J O Udeozo, Roger Unwin, Molly E Wakely, Kenneth Wilde M. T C Wright

The following diplomas and those mentioned in our of April 30 (p 927) were conferred jointly with the Ro College of Surgeons

D C.H —L T Champness
D I.H —Ziauddin Khan
D P H —I H Seppelt

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[1] London Victor Gollancz 1954 Pp 297 15s

oyal College of Obstetricians and Gynaecologists

The following were successful in a recent examination r the diploma in obstetrics:

Jessamine M. Akhurst, James Alexander, H C Allen Anne J derson M. J Barnard, C. T H Barrett Renuka Basu A G yth, J G Blyth Beryl M Bromham J W Brown Jane chanan, C D Campbell Margaret E Chitty, A R Chrispin nor B Clark, Priscilla A Clark Maxwell, J S Clayton Elinor M land, W M D Clements, Mary Clothier W G Cooke R L ppock D C. Cornish Florence M. Cousley P H Crosskey R. Davidson, D W Davis, D A. De Renzy Martin, G W naldson, D M. du Toit, O. E Elliott, Constance H Ellis, Lucy M lis, E. W Evans, Joan M Evans J R Frye H. T Fay Helena M nily Graham Findlay, Kathleen T Flanagan J McC Forrester W Galloway W F P Gammie, R. E M. Geldart, J A Gibson M. Goddard, H. R. Gompertz, J R Gough, Sheila M Gough L. Graham F V Griffiths A. B Guest, A T G Gunn E A ddock, H N Hardy, Adeline K H Heah, John Heffernan, M. Hodges, W S Hossack D S Iles Katherine I Jack abeth M. Jennings, A H John Isabel D Johnson Vivian K. es A R. Jordan Kevin Kelly A. S L Kennedy Father S r Bernard Kirsch, William Lang L A Lees, C S Leithead C Leslie L. R. Lester N H Logan Peter Low R. H Mackay K McAdam Kathleen M. McCartie, Doreen E McConnell F. H. Maeckelberghe J M Manners, Muriel J Martin J F A sell, H McI Morgan Eleanor Morrison, Mary J Mossman A. Naylor Margaret A Norman Jean M North J W Parkin E Partridge W F Paveley, J A Payne Mary Phillips R. Playfair T A Plumley J G Powell, Elizabeth M Price K. Prichard, Margaret J. Purser Olga M Rampersaud, Amla R. n, A. M Reader D M. Reader E. G Rees B F Reichenfeld, alind M. Rewcastle, D P W Roberts Margaret J L Robinson S B Rogers J N Roper A D Rowlands, Hilary M Rowson, rgaret C. Russell Dorothy Sanderson T A. Sanderson, Kenneth ott, R. W Scott, Jane M Scott Brown Jean M Shields, M J R R. Simpson W S Sinton, G H Smerdon R T Smith H Spurway R. M Stanford Hilary K R Steen Phyllis A ens, Audrey B Stevenson Dan Stewart James Stewart, F Stogle, Heather B Thompson John Thompson, David Tingle nmarie D Tupper Jack Walker Patricia G Wallis W W atson, J W S Webb J R. Welsh B F Whiteley, Sheila ldman, Gladys M. H Williams J R. Wood W J Wright, G C. Young

stitute of Cardiology, London

Dr. Lawson McDonald has been appointed assistant rector of the institute

Dr McDonald who is a graduate of the University of Cambridge lified from the Middlesex Hospital London, in 1942 After olding house-appointments there he served in the R.N.V.R. om 1943 to 1946 From 1946 to 1948 he held various appointents at the National Heart Hospital and the Institute of Cardiogy. In 1948 he returned to the Middlesex Hospital as medical gistrar and in 1949 took the M.R.C.P Later he was appointed sistant to the professor of medicine at the Middlesex Hospital, d visited Stockholm in connection with research into peripheral scular disorders He graduated M.D in 1952 He was awarded Rockefeller travelling fellowship for 1952–53 and during its tenure worked in Boston His publications include papers on peripheral scular disease ischaemic heart disease and mitral-valve disease th special reference to the pulmonary circulation and to surgery the mitral valve

ommonwealth Health and Tuberculosis Conference

Mr Iain Macleod the Minister of Health will open this nference at the Royal Festival Hall London, on June 21 her speakers will include Dr Johannes Holm (W.H.O.) r P V Benjamin (India) Prof Etienne Bernard (France) r Walsh McDermott (U.S.A.) Dr E Ross (Canada) r H G Trimble (U.S.A.) Prof Arvid Wallgren (Sweden) r Geoffrey Marshall Dr George Day and Dr Honor Smith. urther particulars may be had from the National Association r the Prevention of Tuberculosis, Tavistock House North ondon, W.C.1

eview of Byssinosis Benefit

The Minister of Pensions and National Insurance has sked the Industrial Injuries Advisory Council to review the rovision made for byssinosis under the National Insurance Industrial Injuries) Acts. This review is being undertaken r the council by their industrial diseases subcommittee The chairman of the subcommittee is Sir Arnold Plant and e members include Prof R E. Lane F.R.C.P

Regulations made under the Industrial Injuries Acts at present ovide insurance cover against the disease for people who have en employed at some time since July 5 1948 and for at least enty years in all, "in any occupation in any room where any ocess up to and including the carding process is performed in ctories in which the spinning or manipulation of raw or waste tton is carried on." Benefit is not, however, available unless the rson concerned has died from byssinosis or his disablement from e disease is assessed at not less than 50% and is likely to be rmanent These conditions were imposed because of the difficulty distinguishing byssinosis from bronchitis and emphysema of non-occupational origin.

Persons and organisations are invited to submit written vidence to the secretary of the council 10 John Adam Street London W C.2 not later than June 6

Institute of Hospital Administrators

The annual conference of this institute will be held at Caxton Hall Westminster S W 1 from May 12 to 14 The principal subject chosen for discussion is Group Administration.

British Association of Physical Medicine

At a meeting held on April 23 the following officers were elected for 1955–56:

President Lord Horder vice president Dr W S Tegner; hon. treasurer Dr A C. Boyle hon secretary Dr G O Storey; hon editor Dr H A Burt

The Medical Sickness Society

On April 26 a reception was held by the Medical Sickness Annuity and Life Assurance Society Ltd. to mark the opening of their new offices at 8 Cavendish Square London, W 1 The guests were received by the chairman, Mr R. McNeill Love

Royal Statistical Society

Study Circle on Medical Statistics—The annual general meeting of this circle will be held on Tuesday May 31, at 5 45 P.M. at the Westminster Medical School, Horseferry Road S W 1 Afterwards Dr P Armitage Dr John Knowelden, and Dr R F Wrighton will read short papers on Controlled Trials in Medical Research

Shortage of Dentists

The Interdepartmental committee under the chairmanship of Sir Arnold McNair, which has been set up by the Minister of Health and the Secretary of State for Scotland to ascertain the reasons for the lack of candidates for training as dentists, has held its first meeting and is ready to receive evidence Persons or organisations wishing to give evidence should in the first instance communicate in writing with the secretary of the committee, Mr T C L. Nicole at the Ministry of Health Savile Row London, W 1

Food Hygiene Advisory Council

On May 2 Mr Heathcoat Amory the Minister of Agriculture Fisheries and Food announced that 11 members of this council are to represent the public 3 the trades, and 3 the workers in the trades. Lord Strong is to be chairman and other members include Mr S W Barnes, secretary to the governors of King's College Hospital Sir Harry Sinderson, F.R.C.P.E director for Sussex of the St John Ambulance Association, and Mrs. James Tweed, chairman of the house committee of St James's Hospital Balham.

Dr Stott Commemoration Fund

This fund has been started as a tribute to the work of Dr L B Stott who until his retirement owing to ill health last December spent 33 years as medical officer at Papworth Village Settlement. In view of his interest in children it is proposed to use the fund for prizes or grants for children at Papworth Village or school and/or a shelter in their playing field

Contributions should be sent to F E Redman secretary of the fund St Peter's Hostel Papworth Everard Cambridge

Haemophilia Society

The annual general meeting of this society on April 24 was attended by 60 members and a number of doctors interested in haemophilia Sir Lionel Whitby F.R.C.P was re-elected president and Dr R G Macfarlane was invited to become a vice president Reports on the work of groups in the South of Scotland Manchester Newcastle Sussex and Middlesex were received During the past year the society had sponsored the formation of similar societies in Australia France Holland, and Switzerland. Its address is 94 Southwark Bridge Road London, S E.1

Hospitals in Eire

The second of three sanatoria which the government of Eire is building was opened at Blanchardstown co Dublin by Mr T F O'Higgins, the minister of health on April 22 The west regional sanatorium at Merlin Park, Galway was opened in 1952 and the southern regional sanatorium will be opened next month The hospital at Blanchardstown will be known as the James Connolly Memorial Regional Sanatorium It has cost £1¾ million, and it will accommodate 520 patients

It is laid out in seven 40 bed pulmonary blocks a 40 bed isolation and infective children's block four 30-bed non-pulmonary blocks (including orthopaedic) and a three-storey hospital and treatment centre with operating theatres and X ray and physiotherapy departments with 80 beds The group of buildings on the 240-acre site also includes a nurses home for 100 nurses and houses and flats for the medical staff

International Society of Criminology

The third congress of this society will be held at Bedford College, London, from Sept 12 to 18, under the presidency of Dr Denis Carroll Further details may be had from the organising secretary, Mr H O Cox, 28, Weymouth Street, W 1

Indian Medical Services Dinner Club

The annual dinner of this club will be held at the East India and Sports Club Ltd , St James's Square, London, S W 1, on Friday, June 10, at 7 30 P M Tickets may be had from the secretary of the club, Medical Board Room, Commonwealth Relations Office, Matthew Parker Street, S W 1

Food Microbiology and Public Health

During its summer conference and annual meeting in Cambridge the Society for Applied Bacteriology will hold a symposium on this subject on July 4 and 5 This is open to non members, and further particulars may be had from Mr G Sykes, the hon secretary, Boots Pure Drug Co , Ltd , Microbiology Division, Nottingham

Kashmir Medical Congress

Arrangements are being made for a party from this country to attend a medical congress in Kashmir next November The approximate cost of £298 per person will include return air fare from London and travelling and living expenses in India Further details may be had from Dr R U Hingorani, 128, Harley Street, London, W 1

International Association of Gerontology

The fourth congress of this association will be held in It early in September, 1957

Vitamin E Congress

This international congress will be held in Venice Sept 5 to 8 at the Cini Foundation on the Island of Giorgio Maggiore Further details may be had from secretary, Prof Emilio Raverdino, Via Pietro Verri 4, Mi

National Insurance Benefits Abroad

People otherwise entitled to National Insurance retire pensions, widows' benefits, or guardian's allowance will able to draw their benefit in any country in the world if dra regulations submitted to the National Insurance Advis Committee are approved At present these benefits ca be paid to people resident abroad only if they are living in the Commonwealth or in the Republic of Ireland

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The British Standards Institution have published a new sta (B S 2606) specifying requirements for flexible lead rubber g for X ray workers Copies of this standard may be obtained fr the institution's sales branch, 2, Park Street, London, W 1, pr 2s 6d

CORRIGENDUM *Hydrocortisone in Lesions of Soft Tissue*—In article by Dr Crisp and Dr Hume Kendall (March 5) the form of hydrocortisone was wrongly given The positions of the –O and – CO CH$_2$OH groups attached to the 17 carbon atom sh be reversed

Diary of the Week

MAY 8 TO 14

Monday, 9th

POSTGRADUATE MEDICAL SCHOOL OF LONDON Ducane Road, London W 12
4 P M Dr R I S Bayliss Infantilism and Dwarfism
ST MARY'S HOSPITAL MEDICAL SCHOOL, Paddington W 2
5 P M Prof F D Moore (Harvard) Endocrinology and Metabolism in Surgical Care (First of two lectures)
INSTITUTE OF CARDIOLOGY National Heart Hospital Westmoreland Street, W 1
9 30 A M Sir John Parkinson Diseases of the Aorta
MEDICAL SOCIETY OF LONDON, 11 Chandos Street W 1
8 45 P M Dr Macdonald Critchley Verbal Symbols in Thought (Annual oration.)
ROYAL FACULTY OF PHYSICIANS AND SURGEONS OF GLASGOW, 242 St Vincent Street, Glasgow C 2
5 P M Dr DeWitt Hendee Smith (Princeton) Ballistocardiography

Tuesday, 10th

ROYAL COLLEGE OF SURGEONS OF ENGLAND Lincoln s Inn Fields, W C 2
3 45 P M Dr H J Hoffman Innervation of Voluntary Muscle (Arnott demonstration)
UNIVERSITY COLLEGE Gower Street W C 1
5 15 P M Dr Mary Pickford Antidiuresis (Cushny lecture)
5 30 P M Prof H C Brown (Purdue University) Proposed Quantitative Treatment of Aromatic Substitution
KING'S COLLEGE, Strand W C 2
5 30 P.M Dr Harriett Ephrussi Taylor (Paris) Induced Transformations of Bacteria (First of three lectures)
ROYAL SOCIETY OF MEDICINE 1 Wimpole Street, W 1
5 30 P M *Experimental Medicine and Therapeutics* Dr Harry Harris Dr J Anderson Dr M D Milne Dr E M. Darmady Renal Tubules
8 P M *Psychiatry* Dr D Russell Davis Dr Norma Kent Mr Richard Lynn, Mr C V Jackson, Mr G Ettlinger Psychological Factors in Educational Disability
WRIGHT FLEMING INSTITUTE OF MICROBIOLOGY St Mary s Hospital Medical School
5 P.M Dr D A Long Response of the Host to Bacterial Infection
INSTITUTE OF DERMATOLOGY, St John's Hospital Lisle Street W C 2
5 30 P M Dr G C Wells Disorders in Pigmentation
UNIVERSITY OF ST ANDREWS Queen's College Dundee
2 30 P M Mr Andrew Logan Dr R M Marquis Prof D M Douglas Consideration of Aortic Stenosis and its Surgical Treatment

Wednesday, 11th

POSTGRADUATE MEDICAL SCHOOL OF LONDON
4 P M Prof. G Payling Wright General Pathology of Tuberculosis (Second of three lectures)
ST MARY S HOSPITAL MEDICAL SCHOOL
5 P.M Professor Moore Endocrinology and Metabolism in Surgical Care (Second of two lectures)
INSTITUTE OF DISEASES OF THE CHEST, Brompton, S W 3
5 P.M Dr F P Lee Lander Prognosis in Bronchiectasis.
INSTITUTE OF DERMATOLOGY
5 30 P M Dr R. W Riddell Pathogenesis of Fungous Infections of the Skin.
NATIONAL INSTITUTE FOR MEDICAL RESEARCH Mill Hill N W 7
5 P.M Prof E L Smith (Utah) Chemistry of Antibodies and Gamma Globulins

Thursday, 12th

ROYAL COLLEGE OF SURGEONS OF ENGLAND
5 P M Mr R V Cooke Advanced Carcinoma of the Co with particular reference to the Inflammatory Fac (Hunterian lecture)
POSTGRADUATE MEDICAL SCHOOL OF LONDON
4 P M Dr C L Cope Cortisone and A C T H
UNIVERSITY COLLEGE
4 45 P.M Prof F L Smith Mode of Action of Proteo Enzymes (First of three lectures)
KING'S COLLEGE
5 15 P M Prof Igino Spadolini (Florence) Effects of the Ace choline-cholinesterase System on the Heart. (Hallib lecture)
ROYAL SOCIETY OF MEDICINE
5 P M *Ophthalmology* Prof J H Dunnington Hyp after Cataract Extraction
INSTITUTE OF DERMATOLOGY
5 30 P M Dr J O Oliver Antibiotics
ROYAL SOCIETY Burlington House W 1
4 30 P M Dr F B Chain F R.S Recent Advances in Ca hydrate Metabolism
ALFRED ADLER MEDICAL SOCIETY
8 P.M (11 Chandos Street, W 1) Dr W P Berring Fugue States
NUFFIELD ORTHOPÆDIC CENTRE Wingfield Morris Ortho Hospital Oxford
8 30 P M Dr A B Kinnier Wilson New Approach to piratory Poliomyelitis
HONYMAN GILLESPIE LECTURES
5 P M (University New Buildings Teviot Place Edinburg Mr G H Macnab Maldescent of the Testicle
UNIVERSITY OF ST ANDREWS Medical School Small's Wynd Du
5 P M Dr H Payling Wright Thrombosis and some less re nised Aspects of Anticoagulant Therapy
UNIVERSITY OF DUBLIN Trinity College
4 30 P M Prof G R. Cameron F R.S New Fields in Pathology (John Mallet Purser lecture)

Friday, 13th

POSTGRADUATE MEDICAL SCHOOL OF LONDON
2 P M Dr J H Middlemiss Radiology of the Acute Abdom
UNIVERSITY COLLEGE
5 15 P.M Dr L E Bayliss Process of Secretion (Cus lecture)
ST MARY S HOSPITAL MEDICAL SCHOOL
5 P M Sir Heneage Ogilvie Shock
INSTITUTE OF LARYNGOLOGY AND OTOLOGY 330, Gray's Inn Road W C 1
3 30 P M Mr A R Dingley Tonsillectomy in Children a Adults
UNIVERSITY OF ST ANDREWS Queen's College, Dundee
2 30 P M Prof. E J Wayne Dr Cecil Pickard Angiocardiography in Congenital Heart-disease

Saturday, 14th

BIOCHEMICAL SOCIETY
11 A M (University of Reading) Scientific papers

Births, Marriages, and Deaths

BIRTHS

LUNTZ —On April 25 at Sorrento Maternity Hospital, Birmingham to Pamela wife of George Richard William Neal Lu M.R C P —a daughter (Verity Anne)

WESTLAKE —On April 25 to Nora wife of Dr E Keith Westlake M D , M R C.P —a sister for Carol Anne (Diana Elizabeth).

ORBITAL LEUCOTOMY

A REVIEW OF 52 CASES

Geoffrey C Knight
M.B Lond F R C.S
RGEON IN CHARGE, SOUTH EAST METROPOLITAN REGIONAL
UROSURGICAL CENTRE ; NEUROLOGICAL SURGEON POST
GRADUATE MEDICAL SCHOOL OF LONDON

R F Tredgold
M.A M.D Camb D.P.M
IONAL PSYCHIATRIST SOUTH EAST METROPOLITAN REGIONAL
PITAL BOARD ; PHYSICIAN DEPARTMENT OF PSYCHO
GICAL MEDICINE UNIVERSITY COLLEGE HOSPITAL, LONDON

m the South East Metropolitan Regional Neurosurgical Centre

In the latter part of 1949 working with Dr Ström sen at the Runwell Hospital one of us (G C K) was le to introduce to this country the operation of orbital dercutting devised by Scoville in 1948 In 10 patients ho had not benefited from leucotomy the operation re results which in Dr Ström Olsen s opinion, justified extension to cases of neurotic tension, in which Scoville d claimed success

During 1950 orbital leucotomy was used in association th Dr Ström Olsen and Dr Bierer and since 1951 re than 50 such cases have been operated on at the uth East Metropolitan Regional Neurosurgical Centre the Brook Hospital Blackheath Elsewhere other difications of the original leucotomy have been per rmed, and Sargant (1953) has drawn attention to their ue He recommended their use in intractable ychosomatic states in anxiety hysteria and in anxiety d depressive states in obsessional personalities ' and pointed out that other forms of treatment notably chotherapy might succeed after operation though y had failed before.

The results *obtained by our modified orbital operation* peared so encouraging as to warrant a closer analysis the patients psychological condition and we have efore collaborated in this interim report The only vious English survey of orbital leucotomy is that of and Lewin (1953) of 20 cases operated on chiefly the late Sir Hugh Cairns at Oxford

Our review covers a consecutive series of 59 patients rred by various psychiatrists, usually because they such anxiety or depression that life was a misery being asked by letter to attend for follow up 4 did not y and remain untraced 3 others had undergone cotomy previously and were therefore excluded from survey Of the remaining 52 40 were British and Polish and all save 4 had been ill for more than two rs—several of them for more than ten years

Basis of Surgical Treatment of Mental Disorder

(G C K)

The surgical treatment of mental disorder began with e injection of alcohol into the frontal lobes and has dually developed into localised anatomico physio ical investigation yielding fresh information about the chanisms of emotion and the intellectual activities the frontal regions. Our knowledge of these matters mains imperfect and the investigation continues.

The effects of the full standard leucotomy dividing central core of white matter within the frontal lobe owed that it was preferable to limit a leucotomy incision the lower segment particularly to the lower and er fibres within the frontal lobe so as to maintain the cessary reduction in emotional tone while minimising associated intellectual deficit

Precise electrocoagulation of the dorsomedial nucleus the thalamus (Spiegel and Wycis 1949) has shown that all the effects of leucotomy may be produced by a lesion strictly localised to one area of the brain from which the afferent connections proceed to the frontal cortex

Our knowledge has been increased by experiments on individual projection pathways either by excision of limited cortical areas (cingulate superior convexity and orbital) by topectomy, and by undercutting similar areas leaving the cortex intact but severing the afferent and efferent fibres passing to and from the selected zones All these methods are intended to modify emotional behaviour while minimising concomitant damage to personality and intellect

Many of these later modifications of technique were developed because of our appreciation of the importance of the thalamocortical connections. Le Gros Clark and Boggon (1933) and Le Gros Clark (1948) have shown that a large part of the frontal cortex is an afferent projection area for the dorsomedial nucleus of the thalamus, comparable with the projection areas of the visual and auditory areas of the cortex, there being a well-defined point to point projection of fibres in which the anteroposterior axis of the dorsomedial nucleus projects in serial order on to the anteroposterior axis of the frontal lobe, to the cingulate superior convexity and orbital surfaces Since the dorsomedial nucleus of the thalamus is essentially a relay station for the transmission of impulses originating in the hypothalamus, the frontal cortex seems to act in part at least as the projection area for fibres concerned with hypothalamic activity and of obvious importance in emotional integration The later developments of surgical technique have concentrated on interrupting certain of these connections alone while leaving the remainder of the frontal cortex undisturbed

Preceding accompanying and giving impetus to these surgical assaults there has been a gradual change in our conception of the nature of intellectual and emotional activity No longer is intellectual function regarded as purely cognitive dependent upon the perfect function of the cerebral cortex working in isolation, and independent of any influence ascending from the basal areas of the hippocampus and hypothalamus, which are concerned in autonomic and emotional activity in the affective sphere It has come to be realised that the function of the cortex *may be profoundly disturbed by stimuli* ascending from the basal areas of the brain

Dana (1921) and Cannon (1927) suggested that emotion resulted from the action and reaction of the *diencephalon* and the cerebral cortex the diencephalon, having received sensory impulses associated with *emotion* would discharge upwards to the cerebral cortex impulses which gave rise to emotional experience or subjective feeling at the same time as it would discharge downwards the motor impulses which produced emotional behaviour

Nathan (1931) held that emotion and personality were localised in the *region of the third ventricle* and traced the development of this theory from the work of earlier observers.

Alford (1933) thought that emotion and consciousness were particularly disturbed by basal lesions in the left cerebral hemisphere

Papez (1937) pointed to the *ensemble formed by the* hypothalamus gyrus cinguli, hippocampus and their various connections, and regarded these as *the probable* anatomical substratum of the emotions. In elaborating this theory he displayed the wide connections that exist between the thalamus hippocampus *and hypothalamus* and between the thalamus gyrus cinguli, and frontal cortex In discussing the hippocampus he pointed to the absence of evidence of olfactory function in this area, and drew attention to the facts *that in rabies* the Negri bodies are most abundant in the large ganglion cells of the hippocampus and the patient shows intense emotion and hyperaesthesia to all forms of stimuli with the result that all stimuli provoke fear sometimes mingled with rage

In Papez's view somatic (including visceral) impulses entering the circuits of these basal areas may obtain emotional colour and finally reach the cortical level as "a stream of feeling" modifying the function of the cortical regions This theory suggests that the pathways connecting the thalamus to the orbital cortex and other regions of the frontal lobe contain the afferent projection systems for emotion, and it is noteworthy that each of the cortical areas receiving such pathways gives rise to efferent fibres passing towards the hypothalamus which could constitute the pathways for *emotional reaction* As Le Gros Clark (1952) has stated

> "It has come to be realised that intellectual and emotional processes are so intimately interlocked in any form of mental activity that it is not possible to separate them even as arbitrary categories Intellectual processes are only capable of normal expression if they are activated and directed by the driving power of emotional processes, The cerebral cortex may be structurally intact but its function can be grossly deranged if it is thrown out of gear with those more primitive parts of the brain which provide neural bases of emotional reaction"

In extending the surgical treatment of mental disorder to the sphere of the neurotic and psychoneurotic it is to the relief of an abnormal emotional charge disturbing the function of intelligence that the treatment appears to be most directly applied We seek a method which will produce the greatest modification of emotional tension without associated injury to intellectual pathways

Scoville (1949) has described the techniques for undercutting each of the three cortical areas—cingulate, superior convexity, and orbital—to which fibres radiate from the thalamus That the orbital technique is the most likely to lower neurotic tension without causing a serious intellectual deficit is suggested by the observations of Rylander (1939) which indicate that lesions of either the orbital or the inferior aspect of the frontal lobes produce changes in emotional tone rather than in intellectual or psychomotor activity Rylander (1952) in particular has shown by psychometric studies that lesions on the superolateral aspect of the frontal lobe are more likely to produce intellectual disturbances Experimental evidence also shows that stimulation of the orbital areas produces autonomic responses, and ablation of those areas tranquillity or loss of fear

Scoville's techniques were fully described and illustrated at the International Congress of Psychosurgery held at Lisbon in 1948, and subsequently published (Scoville 1949) Scoville states that he aims to undercut the entire orbital surface, including the prechiasmatic area, isolating the entire cortex over the orbital plate as far back as the level of the anterior clinoid process on the inner side, and as far laterally as the junction of grey and white matter on the lateral aspects of the lobe We have deliberately modified this method, omitting the lateral portion of the cut and confining the incision to a narrow arc about 2 5 cm wide passing back on the inner aspect of the lobe to a point directly beneath the anter horn of the ventricle at a depth of 5 5–6 0 cm from t frontal pole (fig 1) This modification was introdu to produce further evidence of the importance of t ventromesial fibres within the frontal lobe and to av damage to the hippocampal relays in the lateral portio of the lobe

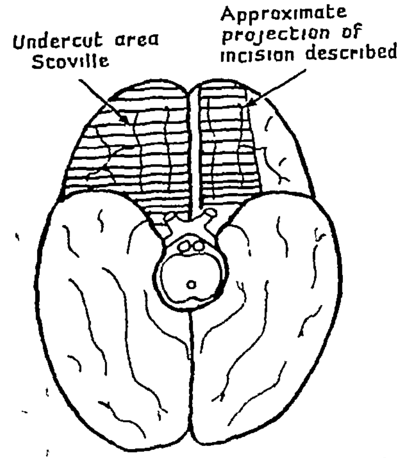


Fig 1—Approximate site and extent of incision in *Scoville's (1949)* undercutting operation and com [illegible] those of incision used in present

Electrocoagulation within the dorsomedial nucleus the thalamus (Spiegel et al 1947) produced bene effects chiefly in the emotional sphere These re are by no means solely attributable to the connect between the dorsomedial nucleus and the frontal pr jection areas (probably hypothalamic connections involved as well), but they do indicate that any signific fibres concerned in emotion and passing to the orb cortex must arise from the inner and lower area of lobe and hence could be divided close to their origin that point

Le Gros Clark (1948), discussing the afferent path from the thalamus, states that projection is well def between certain groups of cells in the dorsomedial nucl and the frontal cortex, fibres proceeding to cortical ar 8–12 approximately in order from the caudolateral part of t dorsomedial nucleus to the anteromedial part of the cort

Meyer et al (1947) concluded that it is the pars ma cellularis of the nucleus that projects on to areas 11 and in the orbital frontal cortex All the fibres projected to t orbital cortex spread thereto from the posteromedial asp of the lobe, and it is this area that has to be cut at the of concentration of the fibres below the pars frontalis o internal capsule rather than the outlying parts of the w matter towards the inferior frontal convolution (fig 2).

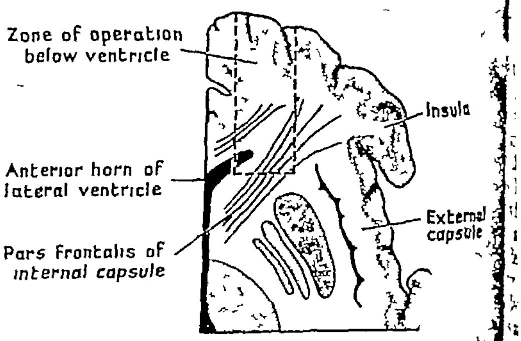

Zone of operation below ventricle
Insula
Anterior horn of lateral ventricle
External capsule
Pars frontalis of internal capsule

Fig 2—Transverse section through right frontal lobe seen from Interrupted line shows zone of operation lying at deeper le ventricle.

Lesions in the lateral aspect of the inferior surface o frontal lobes may *interrupt fibres passing* to the tem pole and hippocampus Efferent association tracts arise area 47 of the frontal lobe (area orbitalis agranularis) w running as the uncinate fasciculus, pass lateral to the ext capsule and radiate to area 38 in the pole of the tem lobe Degeneration has been observed near to or in this fasc by Meyer et al (1947) in post-leucotomy specimens Th fibres form part of a hippocampal circuit involving hi campus, fornix, hypothalamus, thalamus, orbital co uncinate fasciculus, temporal pole, temporo ammonic tr hippocampus, less well recognised than the well known cir hippocampus, fornix, mamillary body, thalamus, gyrus ci hippocampus Positive evidence on the function of th circuits is lacking

It has been suggested that neuronal activity could maintained in a steady state between these circuits long periods, forming a reservoir or background for emot expression Certainly bilateral disturbance of these cir seems to be undesirable

Klüver and Bucy (1939) reported changes in emoti behaviour in monkeys after excision of the temporal lo Hypersexuality has been observed after bilateral dam these circuits Serious results have followed ablation of posterior orbital regions in monkeys (Ward and McCu 1947) with loss of social conscience

Hence, although it has been suggested that tion of the uncinate fasciculus is more importa refrontal leu otomy than sec ion of the thal mocortical fibres, xcept where the im is relief of sceral pain, we mained uncon inced of the dvisability of this ep and decided eliberately to void these lateral d posterior spects of the lobe d so to avoid e possibility of troducing unde able character hanges which ave sometimes en observed in e case of pene ating wounds in at area of the rain

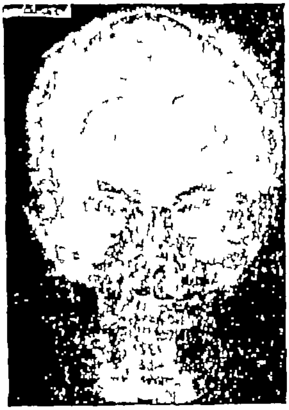


Fig 3—Position of trephine circles for orbital leucotomy

Operation

(G C K)

A transverse scalp incision concealed within the hair e is used the anterior flap being reflected forwards to pose the frontal bones as far down as the level of e orbital margins. A flap of pericranium corre ponding to the exposed area is similarly reflected for ards after mobilisation of the fascia from the line of the mporal crest on each side thus exposing the frontal nes Bilateral trephined circles 3 75 cm in diameter e now fashioned at a point above the level of the frontal nuses and extending to within 1 cm of the midline on ch side (fig 3) The bone-dust thus formed is collected r later use The exposed dura is incised transversely the lower third of the exposed area (fig 4) and stay tures are inserted The frontal pole is raised from the or of the anterior fossa to determine the level of the henoid clinoid process and a transverse incision 2 5 cm. de is made in the cortex hæmostasis is secured and e incision is deepened to the white matter Spatula rceps are inserted into the cortical incision and the hite matter is gradually divided with a fine suction be at the junction of grey and white matter above the bital plate on each side the incision being kept parallel the orbital roof as far back as the level of the tip of e ventricle the spatula blades being used as retractors. ould the tip of the ventricle appear in the line of the cision it is raised with the upper blade of the spatula, d the incision is deepened to a total depth of 5 5–6 0 m beneath the ventricular tip at which level it is dened transversely to 3 0–3 5 cm The incision is actically bloodless, but occasionally bleeding points are seen towards the inner aspect of the incision near the grey matter the bleeding is easily arrested by pressure or by electrocoagulation The dura is now closed with silk sutures and the bone discs are replaced and moulded into position with a paste made from the bone dust The pericranium is brought back into position over the bone discs to conceal any minor surface irregularity, and the wound is sutured in layers

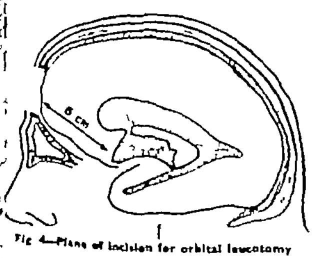


Fig 4—Plane of incision for orbital leucotomy

The postoperative course is smoother than that of a patient who has undergone major leucotomy Incontinence is hardly ever observed There is always a period of drowsiness for the first twenty four hours, and occasionally confusion for the first two or three days, but most patients are fully oriented on the day following operation Within four or five days they can be allowed out of bed, by which time the relief of tension is already apparent The mortality of this operation is obviously low so far more than 75 consecutive operations have been performed without any death

Psychiatric Survey

(R F T)

The survey included : (1) cases seen by me only after operation, and (2) cases seen before and after operation

1 Previous records were studied in detail and compared with the patients present state Since usually no formal or comparable assessment had been made by the psychiatrist who originally referred them it was not easy to be sure that comparisons were reliable ; but, to get as much uniformity as possible the tables of symptoms prepared (see below) were sent back to all these psychiatrists for their comments. In most cases, but not all the psychiatrists had seen their own patients again after operation.

2 These patients were seen immediately before the operation, soon after it and some weeks after it The changes were naturally easier to assess but here also the psychiatrists who had originally referred the patients were asked to comment on the opinions formed Among these patients were 12 Poles who were reviewed in the same way by Dr G Braun of Mabledon Park Owing to language difficulties it was impossible for me to make any adequate assessment in these cases but the criteria had been agreed with Dr Braun

TABLE I—EFFECT OF OPERATION ON SYMPTOMS

Symptom	No of patients with symptoms before operation	Results after operation			
		Much better	Better	Unchanged	Worse
Depression	3[illegible]	[illegible]	8	2	
Anxiety	37	19	11	3	1
Severe insomnia	8	4	4		
Headache	8	[illegible]	5	1	
"Blackouts"	2	2			
Gross lack of confidence	1[illegible]	[illegible]	8		
Lack of interest	18	8	9	1	
Obsessions	13	5	7	[illegible]	
Phobias	4	2	1	1	
Impaired memory	7	[illegible]			5
Impaired concentration	8	1	4		3
Loss of weight	7	7			
Ideas of reference	6	[illegible]	1	[illegible]	

The general results were classified as follows :

A	Markedly improved	23	
B	Some improvement	21	(of whom some are apparently still improving)
C	Unchanged	7	(of whom 3 had shown temporary improvement)
D	Somewhat worse	0	
E	Markedly worse	1	

The various symptoms recorded before operation are listed in table I together with the change after the operation

Besides these symptoms certain others were recorded before operation : rosacea (1), cleared menorrhagia (1) improved ; frigidity (3) improved in 2, but persisted in 1 hysteria (3) persisted ; palpitations (2) persisted and pruritus (2) cleared up

Table I shows that a great improvement was obtained as regards depression, anxiety and loss of weight many patients' interest in their surroundings was restored, and their confidence re established, and, although most of the patients expressed themselves as having some way to go yet, they had also some confidence that they would go this way The effects on failure of concentration and of memory were less good, and these symptoms were in several cases made worse This does not refer to the immediate postoperative period of a week or two, when some impairment of concentration and memory was expected (but passed), but to several months later Nevertheless these symptoms did not appear to cause any great anxiety in the patient No deterioration in personality was evident to me or to any referring psychiatrist in any of those in category A, B, or C

RELATION OF PROGNOSIS TO VARIOUS FACTORS

Previous Personality —Table II shows the cases grouped into various personality types and separated according to their grade of improvement The only conclusion which it seems legitimate to draw here is that hysterical personalities, like hysterical symptoms, offer less ground for hope

TABLE II—RELATION OF PERSONALITY TO PROGRESS

Type	No of cases	Category			
		A	B	C	E
Dependent	14	8	5	1	0
Cycloid	4	4	0	0	0
Obsessional	11	2	6	3	0
Hysterical	5	1	2	2	0
Schizoid	13	6	5	1	1
Psychopathic personality	1	0	1	0	0
Not psychopathic	4	2	2	0	0

Ætiology and Diagnosis —The nature and severity of the psychological factors which had precipitated the illness were investigated but the onset was so long ago that the history given cannot be very reliable In most cases, however, some emotional stress had either caused or precipitated a breakdown Classification being a matter on which psychiatrists notoriously disagree, the symptoms listed in table II and the diagnoses listed in table III may be regarded here with some reserve The 52 cases had, however, been labelled, under the existing nomenclature, and these have been tabulated against their progress It was clear that many cases showed a combination of anxiety with depression, or with obsessional features as table I shows

TABLE III—RELATION OF DIAGNOSIS TO PROGRESS

Diagnosis	Category			
	A	B	C	E
Reactive depression	5	5		
Endogenous depression	2			
Anxiety state	8	2	1	
Obsessional state	2	6	3	
Hysteria	1	2	2	
Schizophrenic state	5	5	1	1
Psychopathic personality		1		

Previous Treatment —These patients had mostly been selected, as noted above, because they had not responded permanently to treatment, but some had previously made temporary progress under electroconvulsion therapy (E C T), and it may be of interest to record the relationship here (table IV), for it is sometimes held that temporary relief from E C T is an indication for operation It seems fair to conclude that the response to E C T gives no indication of what the response to orbital leucotomy is likely to be

Length of History —So far as the records could be obtained, the grades of recovery were grouped against the d[illegible] of the illness (table V) Of the category C patients 2 were hysterics, this is at least as likely a rea as the length of history for their lack of improvem Though it appears that marked improvement is m likely in shorter cases, some improvement may expected from even the longest

TABLE IV—RELATION OF PREVIOUS E C T TO PROGRESS

—	Category			
	A	B	C	E
Previous benefit from E C T	8	7	1	1
No previous benefit from E C T	8	9	3	
Not previously treated with E C T	7	5	3	

Age —The correlation between age and progre given in table VI and does not seem to be significant

NEED FOR SUBSEQUENT PSYCHOTHERAPY

Some of the patients improved so much as to need further treatment, others, notably in categories B C, made less or temporary improvement and appeared benefit from psychotherapy where it was available, was notable, however, that some patients relapsed wh treatment was lacking (for reasons which reflected discredit on anyone), and this point should always considered by the psychiatrist when the patients retu to his care after discharge from hospital.

MAINTENANCE OF IMPROVEMENT

The patients were necessarily seen at different peri after their operation, and observations made on th rate of progress and its maintenance, or of relapse, can readily be analysed The following facts may, how be of interest

TABLE V—RELATION OF DURATION OF ILLNESS TO PROG

Duration (years)	Category			
	A	B	C	E
Up to 5	13	7	2	1
5–10	7	6	1	0
More than 10	1	8	4	0

(1) Some improvement was recorded in most pat within three days after the operation, but 1 patient di improve until seven months afterwards

(2) This improvement went on steadily for several w in most patients, and for months in some

(3) Several patients benefited from postoperative psych therapy whereas previously they had been inaccessible

(4) Nearly all those seen more than a year after operation had remained well since the end of that year

(5) Several patients graded as C (unchanged) had impro but subsequently relapsed

Illustrative Cases

Case 1 —(Reported by Dr JOSHUA BIERER)

A woman, aged 42, when first seen in 1950, complained depression, inability to travel, constant fatigue, dysp palpitations on effort, pains in various parts of the bo gastric disturbances, loss of appetite and weight, constipat insomnia, suicidal thoughts, and anxiety about illnesses as tuberculosis and insanity She seemed to be under g *emotional strain* She answered questions readily appeared to have difficulty over her memory and conce

TABLE VI—RELATION OF AGE TO PROGRESS

Age (years)	Category			
	A	B	C	E
20–30	5	3		
30–40	3	7	3	
40–50	4	5	2	1
50–60	8	4		
Over 60	3	2	2	

on. There were however no signs of hallucination, elusions, or feelings of unreality or depersonalisation

Past History —She had nearly died of pneumonia at the e of 9 and had had a duodenal ulcer while still at school. er appendix was removed at 20

Family History —Her father died at 55 of cerebral hæmor ge, when the patient was aged 17 but the mother lived til 1952 Mother was a very possessive dictatorial woman brother a year older than the patient, to whom she was atly attached was killed in a motor accident before her arriage

Childhood.—She had always been shy timid and reserved t quite normal apart from that. She was so shy that she ed to hide the fact that she was using the lavatory Felt wful' in her first school but felt happier when she changed r school at the age of 15

Sexual History —Menstruation started at the age of 17 xual relations with her husband caused pain and horror ding to frigidity Infrequent throughout marriage, and most ceased after birth of second child

Clinical Assessment —This patient looked younger than her e; her periods started late and her mother suppressed all velopment towards independence. The patient sought to d her independence in her married life but was too immature take any responsibility She expected pleasant feelings, fection, love, and security but instead she experienced orror and insecurity her husband being financially unreliable Having been used to complete dependence and having pected freedom from what she experienced as slavery she lt cornered. This caused such tension most of the time that en the security of nursing home specialists, and large doses f barbiturates did not bring her any relief Electroplexy d prolonged narcosis, like any form of psychotherapy ought her only a very temporary relief Life to her her mily and her doctors became unbearable

Progress —She postponed the operation twice because lations advised her against it in the end she agreed, and bital leucotomy was performed in May, 1951 She was sent r six weeks convalescence; she hated the place she was nt to the food, and the company She returned to work in r home rather too soon, according to her own statement

Effects —This emotionally and otherwise immature patient ho showed marked depressive hysterical and hypochondriacal symptoms of long standing who underwent and used others unbearable suffering was completely relieved y the operation and enabled to live a normal life again is was achieved with so little personality change that it d not interfere with her life Two years after the operation e described her state as a wonderful feeling' She had no mplaints, except sometimes slight nervous depression. All r tension has gone she can run her house and travel any here (which she could not do before) She enjoys going to the atre though she does not get the same thrill out of it

Case 2 —(Reported by Dr G BRAM)

A woman, aged 40 was admitted to Mabledon Park Hospital n June 27 1951 with delusional ideas of persecution pression and emotional instability

History —Apparently she was in good health until August, 44 when she was wounded by a shell splinter in the right rietal occipital region She was unconscious for several urs. For four months after being wounded she had left d paresis, and later she developed pain in the left shoulder d arm which did not respond to any analgesics.

Course of Illness.—On admission in 1951 she was apathetic d depressed and expressed delusional ideas of persecution; he said that the pain in her left shoulder and arm was caused y some electric currents used against her by unknown eople Three weeks after admission she refused to eat nd had to be artificially fed She had twelve electroconvul ons with very good response She became symptom free nd the pain in the left shoulder and arm completely subsided. he remained well for five months and then relapsed displaying he same symptoms as before A further course of E C T was iven but without any improvement

Orbital leucotomy was done in October 1952

Effects —The patient made remarkable progress and was ischarged in full remission four months later (the pain in he arm was no longer present) When she was readmitted for few days in September 1953 for review it was found that he had fully maintained her remission She can look after erself and do part time work The pain in her left arm had ever returned.

Case 3 —(Reported by Dr M WATSON and R F T)

A woman was first seen in 1952, at the age of 55 She had had depression since June 1949 fluctuating in intensity It had improved somewhat with E C T (but this produced so much panic that it was stopped) and with œstrogens and dexamphetamine but she had always soon relapsed. She had a demanding and sick husband and a daughter with disseminated sclerosis One suicidal attempt Her depression was associated with guilt indecision and feelings of emptiness in her head some paranoid ideas; short occasional hypomanic phases with gross extravagance

Past History —Subtotal hysterectomy at the age of 42. No menopausal symptoms Left mastectomy at 43 for carcinoma.

Family History and Childhood —Apparently happy relationships with no relevant incidents. Husband a war pensioner now unreasonable and doing no work Five daughters.

Orbital leucotomy in March, 1952

Effects —Much improved twenty five days after operation and steady progress until seen eighteen months later except for two interludes—a gross obstructive jaundice in July 1952 and a short phase of laziness and aggressiveness in December, 1952 The jaundice was completely painless and a secondary carcinoma was suspected but it cleared up in three weeks and was apparently an infective hepatitis In November 1953 she had no complaints, being cheerful and placid, but not unduly so She was quite rational, coöperative, and capable of coping with the domestic stress which still persisted She regarded the change in herself as wonderful

Conclusions

The criteria used to select these patients had not been carefully defined beforehand, but clearly most of them had severe anxiety or severe depression They had long records of illness and misery (misery which affected their families too) *no previous psychotherapy had been of* avail E.C T had given little relief, and surgery was their last hope In these circumstances a high percentage of success would scarcely be looked for

This being so the success of the operation seems remarkable 23 out of 52 were markedly better, 21 somewhat better and only 7 unchanged Only 1 was worse in general, and though a few had greater difficulty in concentration or memory even these regarded themselves as better and happier A deterioration of personality was recorded in only 1 case

Though no sweeping conclusions can be drawn in an interim report on so small a series, these results suggest that orbital leucotomy should be seriously considered in long-standing severe anxiety states and depressions which do not respond to psychotherapy

It is not yet possible to say which patients will benefit most. Previous response to E C T offers no guide to prognosis nor does age The results seem more hopeful if the duration has been less, as might be expected Cases with hysterical symptoms do not seem to be suitable for the operation

All cases should be reviewed by their original psychiatrist after the operation Some patients need further psychotherapy and will benefit from it even if they did not before

We are much indebted to our neurosurgical colleague Mr G Northcroft for preparing the accompanying diagrams We would like to express our gratitude to all the psychiatrists in this region who recommended patients, supplied information and checked the assessment made later; and in particular we wish to thank Dr Bierer and Dr Bram for more detailed assessment and for permission to publish in detail the findings in cases 1 and 2

REFERENCES

Alford L B (1933) *Amer J Psychiat* 12, 789
Cannon, W B (1927) *Amer J Psychol* 39 10
Clark, W E Le G (1948) *Lancet*, i 353
— (1952) Prospects in Psychiatric Research (Proceedings of Oxford conference of Mental Health Research Fund) p. 5
— Boggon R. H (1933) *Brain* 56, 83.
Dana, C L (1921) *Arch Neurol Psychiat., Chicago* 6 634
Klüver H Bucy P C (1939) *Ibid* 42 979

References continued overleaf

UNDERCUTTING OF ORBITAL CORTEX IN CHRONIC NEUROTIC AND PSYCHOTIC TENSION STATES

R STROM-OLSEN
M D Wales, B Sc , D P M
PHYSICIAN SUPERINTENDENT

D W C NORTHFIELD
M S Lond , F R C S
NEUROSURGEON

RUNWELL HOSPITAL, WICKFORD, ESSEX

THE risk of personality defects has deterred many from applying leucotomy in chronic neurotic and other tension states (Strom-Olsen 1946) The patient with a well-preserved personality is likely to show greater loss than one with a simple and shallow personality (Ström-Olsen and Tow 1949) , and, though standard leucotomy can be justified for a chronic disturbed psychotic who usually shows much deterioration, it is in our opinion inadvisable for the person with an intractable neurosis A different operation was therefore required for cases of chronic anxiety, obsessional neurosis, and hypochondriasis, and for some cases of paranoid psychosis and chronic depression which do not respond to electroconvulsion therapy (E C T) or other treatment

TABLE I—CATEGORY A

Case no	Diagnosis	Duration of illness before operation (yr)	Length of follow up after operation	Result
1	Chronic anxiety state	5	4 yr	Recovered
2	Chronic hypochondriasis	15	$3^{1}/_{4}$ yr	Recovered
3	Chronic anxiety state	8	$2^{3}/_{4}$ yr	Improved
4	Chronic hypochondriasis	11	$2^{3}/_{4}$ yr	Improved
5	*Psychopathic* personality and drug addiction	8	$2^{1}/_{2}$ yr	Improved
6	Paranoid schizophrenia	5	2 yr	Recovered
7	Chronic hypochondriasis	20	2 yr	Improved
8	Chronic anxiety state	4	2 yr	Recovered
9	Chronic endogenous depression	$3^{1}/_{2}$	$1^{3}/_{4}$ yr	Recovered
10	Paraphrenia	5	$1^{3}/_{4}$ yr	Improved
11	Chronic anxiety state and depersonalisation	$3^{1}/_{2}$	1 yr	Recovered
12	Chronic melancholia	10	$5^{1}/_{2}$ mos	Not improved, died
13	Chronic depression	3	5 mos	Recovered

The method of selective cortical undercutting devised by Scoville (1949) was adopted at Runwell Hospital in January, 1950 Mr Geoffrey Knight, then neurosurgeon to the hospital, was the first to perform the operation in this country, and he operated on the first 9 cases, which are not included in the present series

In view of the experience of Scoville (1949) and Rylander (1951) the selective undercutting operation has been restricted to the orbital cortex We have no experience of undercutting either the cingulate area or the superior convexity of the frontal lobe

Material

The series consists of 27 patients operated on January, 1951 They fall into two categories (and II)

A. Patients with well preserved personalities who suffe from long standing tension states, depression, or other e tional distress which had completely incapacitated th Each had received other forms of treatment without perma beneficial results

B Chronic disturbed psychotics, usually schizophre who already showed considerable deterioration and in w the aim was a nursing improvement rather than a cure

Serious postoperative defects would be discerned rea in the first group, but less readily in the second

Of the 27 patients 8 were men and 19 women 3 m and 10 women in category A, and 5 men and 9 wome category B Their ages ranged from 23 to 61 years, being between 23 and 40, and 10 between 41 and 61.

Operation

The operations have been carried out under gen anæsthesia and along the lines described by Sco (1949) and by Tow and Lewin (1953)

It has not been found necessary to use a trephine la than $1^{1}/_{4}$ in in diameter, and this size is much easier to manip late than a larger one The *trephine is placed so as to br* the edge of the opening in the skull as close as possible to th orbital roof, and about 1 cm either side of the middle line. I some cases the frontal sinus has been traversed , when th has happened, the mucosa of the sinus has been tur inwards towards the nasal duct, and the mouth of the cavit lightly packed immediately with 'Gelfoam' liberally p dered with penicillin and sulphathiazole , any separ portion of mucosa attached to the disc of bone has b entirely removed, and the overhanging lip of bone (for the detached posterior wall of the sinus) has been nib from the disc In such cases prophylactic penicillin is g for five days after the operation, and no complication followed the opening of the frontal sinus

During the closure of the wound the discs are sutur place, and the crevice which surrounds the replaced dis filled with bone dust , this prevents the unsightly defor which may become apparent some months after the opera when the scar tissue contracts and reveals a circular groo the site of each trephination

Provided the trephine openings are low in the frontal the tip of the frontal pole will be exposed after incisi dura mater, and the lightest degree of retraction will one to elevate the frontal pole so as to bring the optic n into view at the point where it enters the optic foramen, on each side to measure its depth from the anterior surfa the pole This is the depth to which the "cut " should

TABLE II—CATEGORY B

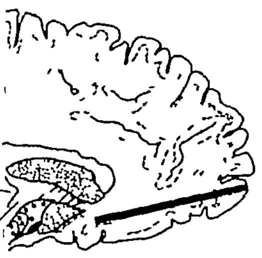
Case no	Diagnosis	Duration of illness before operation (yr)	Length of follow up after operation	Result
14	Paranoid schizophrenia	6	$2^{3}/_{4}$ yr	Improved
15	Paranoid schizophrenia	$7^{1}/_{2}$	$2^{3}/_{4}$ yr	Improved
16	Paranoid schizophrenia	9	$3^{3}/_{4}$ yr	Improved
17	Chronic schizophrenia	10	$2^{1}/_{2}$ yr	Not improved, died of intercurrent disease
18	Paranoid schizophrenia	$3^{1}/_{2}$	$2^{3}/_{4}$ yr	Not improved, subsequently had standard leucotomy
19	Paranoid schizophrenia	36	$2^{3}/_{4}$ yr	Improved
20	Catatonic schizophrenia	17	$2^{3}/_{4}$ yr	Not improved
21	Paranoid schizophrenia	$4^{1}/_{2}$	$2^{1}/_{2}$ yr	Improved
22	Hebephrenic schizophrenia	$3^{1}/_{2}$	$2^{1}/_{2}$ yr	Not improved
23	Chronic paraphrenia	$8^{1}/_{2}$	$2^{1}/_{4}$ yr	Improved
24	Schizophrenia	7	$1^{3}/_{4}$ yr	Recovered
25	Catatonic schizophrenia	6	$1^{3}/_{4}$ yr	Improved slightly
26	Catatonic schizophrenia	4	$1^{1}/_{2}$ yr	Unchanged
27	Paranoid schizophrenia	15	10 mos	Improved

MR. KNIGHT, DR TREDGOLD REFERENCES—*continued*

Meyer A Beck E McLardy T (1947) *Brain*, 70 18
Nathan, M (1931) *Pr méd* 39, 857
Papez J W (1937) *Arch Neurol Psychiat* , *Chicago*, 38, 725
Rylander G (1939) *Acta psychiat suppl* 20 p 3
— (1952) *Congr int Psychiat Neurol* 4 356
Sargant W (1953) *Brit med J* ii 800
Scoville, W B (1949) *J Neurosurg* 6 65
Spiegel E A Wycis H T (1949) *Proc R Soc Med* 42, 84
— — Marks, M , Lee A. J (1947) *Science*, 106 349
Tow P M. Lewin W (1953) *Lancet* ii 644
Ward, A McCulloch W S (1947) *J Neurophysiol* 10 309

ade and should not be transgressed If necessary the [illegible] arachnoid can be broken and cerebrospinal fluid moved by suction to gain extra room. The brain is now lowed to resume its normal position and a suitable site on e frontal pole is chosen for the cortical incision which runs ansversely for the full diameter of the opening in the bone d approximately parallel to the roof of the orbit The ecise position of the incision depends on that of veins d on the cortical pattern large veins should be avoided if sible, and an incision through the summit of a gyrus avoids all arteries hidden in sulci The obliteration of a large vein y give rise to local congestion, making the operation more ficult. The cut is now made into the brain in a plane rallel to the orbital surface of the frontal lobe and about m. under it. The correct direction is repeatedly verified by moving the spatula or other instrument used for the dissec n, and reorientating oneself in relation to the roof of the bit. As the cut is deepened a narrow retractor is held so as maintain the orbital surface of the brain against the orbit hen the required depth has been reached (centimetre kings on the retractor are a great help) the cut is gradually tended medially until one estimates that the middle line s been nearly reached, and then laterally until increased sistance indicates that the lateral cranial wall is being proached.

Hæmorrhage in the depths of the cavity is controlled by e common neurosurgical methods, which are used until gentle irrigation reveals that hæmostasis is satisfactory The under surface of the frontal lobe is now re-examined to make sure that no unsuspected hæmorrhage has taken place on the outside of the brain the dura mater is approximated with silk and covered with a piece of gelfoam



1—Sagittal view of brain 1 cm. lateral to line showing usual position of lesion in orbital undercutting: IC, internal capsule; thalamus. (Tracing from myelin-stained ction.)

It is essential that anæsthesia should be induced and maintained expertly so as to avoid all cerebral congestion due to ory obstruction, cyanosis or retention of carbon dioxide he brain bulges when the dura mater is opened one should it for this to subside, checking for possible defects in the ministration of the anæsthetic in these circumstances it is er to postpone operation than to attempt undercutting

The position of the head is important; if it is moderately ended the weight of the brain causes the frontal lobe to fall ay slightly from the roofs of the orbits, thus reducing the ree of retraction necessary

Orbital undercutting is a delicate operation which annot be performed hurriedly It demands a much gher standard of technical skill and attention to detail han does leucotomy and should never be undertaken ithout the full panoply of neurosurgical assistance and paratus Inspection of the specimen (figs 1–3) has mphasised the narrowness of the margin between the sterior part of the orbital cortex and the inferior pect of the anterior extremity of the caudate nucleus At this depth deviation from the correct plane must learly be very easy and damage in either direction or at oo great a depth may lead to fatal consequences.

Results

Category A.—Of the 13 patients in this category 7 ave recovered 5 have improved and 1 has shown no hange Of the 12 recovered or improved 9 have been ischarged from hospital 7 of them are living normally t home and working for the first time in many years; he remaining 2 are free from symptoms and are steadily mproving but have not yet fully adapted to the stresses of life outside hospital These patients have experienced marked subjective relief of their emotional tension, distress or aggressive tendencies, according to the diagnosis Experience has shown that improvement in social adaptation may continue up to two years after discharge

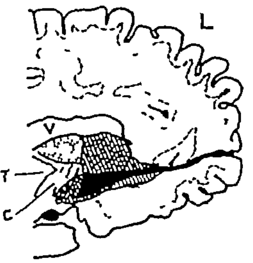


Fig. 2—Comparable (same scale) sagittal view of brain of case 12: IC internal capsule; T thalamus; V ventricle; black complete loss of tissue; hatched partial loss of tissue. (Tracing of fixed brain.)

Category B.—As was to be expected the results in this category are less favourable Only 1 has shown a social recovery but improvement has been evident in 8 of whom 4 have been discharged to their homes. This improvement has been greatest in patients who suffered distress because of hallucinations or displayed impulsive and violent behaviour However, our experience leads us to believe that undercutting of the orbital cortex is insufficient for the more severe schizophrenics because one such patient had afterwards to undergo a standard leucotomy Of the 4 chronic psychotics who were discharged 1 schizophrenic made a social recovery and has started working for the first time for many years, 2 have been relieved of their psychotic symptoms (1 is working full time and supporting her family, and the other lives a fairly normal existence and does some housework) the 4th patient, a young schizophrenic was discharged against advice and has not shown any improvement.

In both categories those patients remaining in hospital who were classified as improving have had considerable relief They are now nursed in better wards and can enjoy more freedom within the hospital

Postoperative Complications

There were no cases of clinically recognisable cerebral hæmorrhage following the operation Patient 5 in category A had epileptiform fits on the second day after the undercutting but has had none since Patients 2 and 8 in category A developed complete loss of the sense of smell, presumably through injury of the olfactory bulb tract or cortex. Patient 20 in category B had hyperpyrexia and coma for forty-eight hours but made an uneventful recovery

Incontinence of urine so distressing in many post leucotomy cases, is occasionally met with during the first

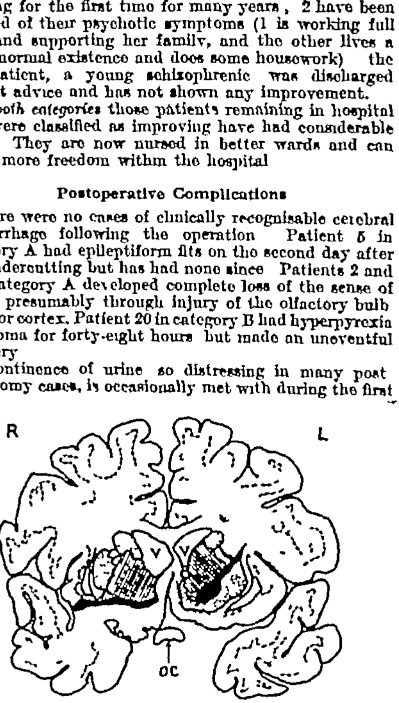


Fig 3—Coronal view of brain of case 12 at level of optic chiasma: OC optic chiasma; V ventricle; black, complete loss of tissue; hatched partial loss of tissue. (Tracing of fixed brain.)

week or two following orbital undercutting but has never persisted Except in patient 12 in category A, there were no serious or permanent postoperative complications This is in marked contrast to the standard leucotomy

Postoperative Personality Changes

The 27 patients have been thoroughly investigated for postoperative personality change, and the 24 who proved coöperative have also undergone psychometric tests by Dr Graham Foulds The 13 discharged patients have been followed up in detail at regular intervals, and not only have the relatives and the patients been interviewed, but in all cases the homes have been visited by one of our psychiatric social workers and sometimes also by one of us Special importance was attached to statements by relatives, not only on the improvement they noticed in the mental picture but also particularly on the development of undesirable symptoms In this respect the difference between the present patients and those who have undergone standard leucotomy is very striking Except patient 12, none of those in category A has shown any serious personality defect The same is true of the chronic psychotic patients, category B, though here it became less easy to distinguish between deterioration of the personality due to the psychosis and deterioration due to the operation Compared with changes seen after standard (or medial) leucotomy, there have certainly been no serious or unpleasant psychological or behavioural sequelæ There is, in our opinion, a quantitative rather than a qualitative difference There is some loss of spontaneity, which tends, however, to lessen as the months go by Some patients complain of an abnormal tiredness for the first few months Although abnormal emotional tension is eased, there is little blunting of affect—certainly never to the point of apathy For the first few weeks there is a tendency to emotional facility, with at times outbursts of laughter for little apparent reason, but this symptom has always subsided In the social sphere the recovered patients are able to work efficiently and enjoy their pleasures, contrasting vividly with post-leucotomy patients 2 of the chronic psychotic patients appeared to develop increased sexual drive However, in one of these cases there was evidence of eroticism before the undercutting It may well be that inhibition diminished

24 patients were tested psychologically four weeks after operation and 12 were tested again six to twelve months after operation The tests included Mill Hill vocabulary scale, progressive matrices, porteus mazes, thematic apperception test, Rorschach test, and Wechsler Bellevue test The outstanding features of the results so far obtained is their constancy and the absence of any sign of intellectual deterioration On the credit side are improvements in appetite, sleep, and sociability, thus patient 5 in category A, who had for years been habituated to amylobarbitone, could take little food, and was in danger of dying from starvation, quickly regained her appetite, put on weight, and could do without night sedation

Complications due to too Posterior Cut

Case 12 in category A—that of a woman of 54, with ten years' melancholia—demonstrates the danger of a lesion extending too posteriorly

After her undercutting operation in May, 1954, she was extremely drowsy for an abnormally long time She had to be fed and was incontinent She showed complete apathy, had a mask like expression, and developed signs of bilateral pyramidal damage and parkinsonism, she could not walk or stand The blood protein picture showed an absolute increase of globulin (total serum protein 6 3 g per 100 ml, albumin 2 2 g, globulin 4 1 g, albumin/globulin ratio 0 54) Within the globulin fraction the α_1 component showed a significant increase over the normal values The blood levels of urea, sodium potassium, calcium, magnesium, and chlorides were all normal, as was the CO_2 combining power The most striking feature, however, was intractable trophic ulcers both shoulders, the outer edges of both feet, the sacrum buttocks, the trochanters, the big toe joints, both heels, left external malleolus, the left fifth toe, and the left Some muscles and tendons had been eroded right thro and even the great trochanter had been eroded These ul were severely infected

In spite of intensive treatment the patient gradually deteriorated, lost weight, and eventually died, five and a h months after operation, from pneumonia, septic absorp and cachexia At necropsy (Dr J A N Corsellis) the bra weighed 930 g, on both sides the surgical lesion had extend through the head of the caudate nucleus, the putamen the related segment of the internal capsule (solid black in fig 2 and 3) The area of partial damage however (as shown b hatching) appeared to be secondary and due to interference with the blood supply

In this case, it will be noted, the brain was abnormally small, and this may well explain why the section w carried too far back from the frontal pole Similar ca of severe trophic disturbances have been described following leucotomy where the cut has been made mo posteriorly than normally (McLardy 1950)

Illustrative Case-reports

Case 1 —A man, aged 34, was admitted to Runwell Hospi because of anxiety with nervous vomiting, which began dur convalescence from pulmonary tuberculosis in Septemb 1950, and was causing physical deterioration He had alw been a nervous and sensitive person and had had bronchi asthma since the age of 9 In 1946 he was discovered to h pulmonary tuberculosis and received sanatorium treatm until October, 1949 Severe anxiety symptoms began when h began to get up from a course of rest in bed. He felt afraid leaving his bed, had a sensation of "nervous tension in t solar plexus," and would vomit, at first when anyth untoward happened, and then after meals regularly two three times a day He was preoccupied with the idea that h tuberculosis would break out again at any time, and att of asthma, which had been rare while he was in the sanator began to recur frequently

When admitted he had already lost 21 lb Psychother and sedation failed to produce any improvement Sh after admission the tuberculosis was found to be active more, and he was treated by chemotherapy He bec increasingly anxious and vomited so much that it was im sible to continue giving him *p* aminosalicylic acid, and h dietary intake was quite inadequate It was decided th orbital undercutting, while his general condition rem good enough to permit the operation, was the only treat open, and the operation was performed under general an thesia in January, 1951

Progress After Operation —With continued chemother recovery from operation was uneventful After a week th patient appeared more calm, did not complain spontaneo of his fears, and took his diet well, though he denied improve ment when questioned There was a gradual over all improve ment in his anxiety symptoms during the following mont except for two transient re-exacerbations of fear and vomit eight and ten weeks after operation, which did not interf with the steady improvement in his pulmonary conditio Eighteen months after the operation he was ambulant, n longer afraid of exertion, optimistic about the future, a making plans for a return to normal life He was still slight anxious about meals, and feared a return of vomiting Unfor tunately a series of upper respiratory tract infections delaye his discharge from hospital for some months, but he continued to gain confidence and was fit for discharge twenty two mont after operation. There was no return of the vomiting, and h was eventually sent to a tuberculosis rehabilitation unit, wher he started work as a welfare officer, driving his car abou without any symptoms of fear or anxiety

Follow up —When seen nearly three years after the opera tion he had been disabled through an attack of asthma bu was now well and was going back to his job He admitted that he was vastly improved and could do his work as far a his chest condition would allow him He was cheerful and there was no evidence of tension His parents stated that th could not see any detrimental traits following the operatio

Case 2 —A woman, aged 59, who had had two previo admissions to Runwell Hospital, was admitted for the th me in November 1951 The history of her neurosis went back for at least fifteen years and she was almost completely incapacitated. She had depression anxiety and agitated hypochondriasis She was given various forms of treatment including E.C.T with no improvement She spent most of her time in bed and, when at home could barely help with any housework, at times having to crawl about on her hands and knees.

On admission she was tense agitated and hypochondriacal with severe insomnia severe pains in the abdomen and head weakness of the legs palpitations and pains in the chest She was preoccupied with her symptoms to the exclusion of anything else She swayed about, wringing her hands and moaning continually asking for sleeping-drugs to ease her The symptoms had gradually got worse during the three or four years before admission but were essentially the same as though rather less severe than when she was first seen at the outpatient clinic in 1937 Bilateral undercutting of the orbital cortex was performed on Dec 24 1951

Progress After Operation.—For the first four days she was somewhat drowsy and was unaware that she had had an operation. Ten days afterwards she was placid and cheerful, with no agitation. She no longer spoke in a whining voice and hand-wringing was absent She could smile and laugh and said she felt much better There was no incontinence but she was rather slow in eating her food During the following two months she steadily improved and in March, 1952, she was discharged symptom free

Follow-up —She has been visited in her home several times since and her son also has been interviewed When last seen three and a quarter years after operation she was doing all her cooking and housework. Whereas previously she never got up until 12 or 1 o clock, she was now up by 7 A.M She went out two or three times a week and had taken up her hobbies again. She said: "There is a vast improvement in me I can now sleep without drugs, I am not a bit depressed all those dreadful sensations are gone She read good books and had no difficulty in concentration Physically she was stronger and had put on some weight

Case 6.—A woman, aged 38 at the time of operation had had paranoid schizophrenia for four years, during which she had been admitted three times to hospital At first her illness was characterised predominantly by apathy withdrawal and inaccessibility She had auditory hallucinations and delusions of a persecutory nature—e g that she was always being watched by radio and television and that someone else came into the house to usurp her place whenever she went to bed or went out. She believed that her husband was unfaithful to her and she was frigid towards him and she lost interest in her children. She was disconnected in conversation and showed thought blockage Eighteen months before operation she began to be aggressive and attacked her husband and the nurses. She became increasingly violent and impulsive apparently in response to hallucinations. Orbital undercutting was performed there was excessive bleeding at operation, and generalised epileptiform convulsions came on that evening She was incontinent for six days but after this convalescence was smooth

Progress After Operation —A week after operation she was still extremely apathetic but was coöperative and denied having hallucinations. After a month she was showing more interest in her surroundings, attending occupational therapy helping with light duties on the ward and keeping herself presentable She remained cooperative and well conducted and conversed freely There was no tension and no evidence of hallucinations nor did she voice any delusions. She went home three months after operation and was discharged after a further five weeks. At home she took up her duties in the house and looked after her children, and relations with her husband became satisfactory

Follow up —Seen about twenty-one months after the operation she remained very well She was contented and there was no evidence of tension or hostility or of delusions or hallucinations; these had petered out Marital relations with her husband had become perfectly normal. She was now doing most of the housework cooking and cleaning though she did not often go shopping She had become affectionate towards her husband and children. She did not tend to lie in bed in the morning but made an early start with her housework. The husband remarked that the only thing he noticed wrong was that she could not plan things well sometimes showing lack of foresight but apart from that he regarded her as perfectly normal.

Case 8 —A woman aged 34 had had a chronic anxiety state with panic attacks for four years Depression and anxiety had been developing since early 1949 before which she had had a well integrated personality and held responsible executive posts She improved somewhat at first and left hospital in July 1950 only to be readmitted in April 1951, with an exacerbation of anxiety and panic attacks She was now extremely tense and trembly showing tachycardia and complaining of pains in the chest weakness of the legs and loss of energy and self-confidence In spite of sedation and psychotherapy she did not improve She had slight myxœdema following a thyroidectomy, but this was kept well under control with small doses of thyroid. For the next two years she continued in more or less the same condition. She was often lacrimose easily upset and complaining of constant fears No physical treatment improved her condition She was restless, irritable and at times excitable and she continually complained of tiredness She underwent an orbital undercutting operation in April 1953

Progress After Operation —Immediately afterwards she was completely relaxed and at ease There was no evidence of depression and the crying bouts ceased She was amnesic for the operation She continued to make good progress, and four months after the operation she was discharged and went to live with a friend who knew her very well.

Follow-up —She has been seen on numerous occasions, and her social recovery has been maintained for the past two years Unfortunately she has severe purulent sinusitis which gives rise to headaches and muzziness At times she is anxious about her health but this appears to be a normal reaction. Her friend is extremely pleased with the result The patient looks much better physically She can do her shopping though she cannot do her work. She still complains of tiredness and lethargy but she mixes much more socially with other people and remains quite free from neurotic symptoms.

Case 9 —A woman aged 50 began to have chronic melancholia at the menopause three and a half years before operation Her previous personality was over-conscientious and rather obsessional Five months after cessation of her periods she was admitted to the hospital under certificate after a suicidal attempt with aspirin She was depressed and expressed numerous delusions of guilt—e.g that she was contaminating all those around her and that she was the source of all the cancer tuberculosis, and blindness in the world. She had auditory hallucinations and heard people accusing her of sexual misdemeanour At this time she was experiencing menopausal vasomotor symptoms. Although she responded well to convulsion therapy she relapsed within a few months and after the third course of treatment the remission lasted only ten weeks. Recurrence of depression was accompanied by retardation: she lost all interest in life and in her relatives felt that all contact with other people was wicked and refused her food At the time of orbital undercutting she had been continually depressed for ten months

Progress After Operation —A week after operation she showed clear improvement. She was only mildly depressed showed affection for her relatives and took her diet with little persuasion Improvement continued and melancholic symptoms gradually faded out Two months later she was cheerful and active, eager to help with work on the ward and sociable and she liked to attend all the social functions in the hospital though she still occasionally expressed self accusatory delusions. She left hospital on trial and was discharged five months after operation.

Follow up —She has been seen regularly at home where she lives with her sister and as an outpatient during the year that has elapsed since her discharge and has remained quite well She shows no depression or delusions is active neat and tidy (still having a keen regard for cleanliness and orderliness) and feels capable of doing her share of household duties and shopping She likes to go out a good deal and enjoys radio and television though she finds her interest in reading somewhat diminished. Her sense of smell is absent since the operation. She looks considerably younger and smarter than before

Case 11 —A woman, aged 29 had had severe anxiety symptoms with depersonalisation for two and a half years before operation Her illness began suddenly after a minor bicycle accident in which she was not injured She was anxious and afraid to leave the house and to stay in the house by herself and she could not believe in the reality of [illegible] ment or in her own reality She could not do [illegible] and was continually preoccupied with her symptoms She was admitted to other hospitals on three occasions before her admission to Runwell Hospital and had received various courses of treatment, including E C T and insulin therapy, without relief from her symptoms Observation for nearly a year before operation showed her to be continually complaining of the symptoms and importuning for reassurance about her unreal feelings "Am I alive, or am I dead? Is it today? When will things look real?" She said she could not think of anything else or enjoy any activity There were periods of agitation when she was unable to sleep, and she took little interest in her appearance

Progress After Operation—After operation she was no longer agitated, slept without sedation, and was free from feelings of unreality, she kept herself well occupied with ward work and occupational therapy, and took full advantage of social facilities She conversed freely and easily, laughed, and enjoyed herself She was discharged six weeks after operation and at once took up her management of the home and her old interests

Follow up—She and her husband were seen separately three and a half months after discharge She had put on weight, previously having been thin and undernourished She looked considerably younger Her husband said there was a dramatic improvement There was no agitation or depression She was looking after her home very well and getting up early She no longer presented any symptoms of depersonalisation and had not once asked for reassurance She found that her housework was not quite enough and would like more to do She had normal initiative She enjoyed such entertainments as cinema, radio, and dancing, and there was no evidence of impairment of drive or concentration At times she complained of tiredness, but this in no way interfered with her activities She has now obtained employment and is working full time

Case 13—A dock labourer, aged 31, had depression with paranoid delusions for three and a half years before the operation Previously he had enjoyed excellent health except for an accident at the age of 30, when he fell 60 feet, fracturing his spine and wrist, without persisting disability At the onset of his mental symptoms he would return from work morose and disgruntled and would sit brooding for hours Shortly after this he expressed paranoid ideas about his work-fellows, became increasingly agitated, depressed, and sleepless, and believed that men were surrounding the house, talking about him, and trying to get in at him This culminated in his admission to hospital after attempting suicide by cutting his throat

On admission he was tense, depressed, and retarded, with little spontaneous activity, and showed a tremor of his hands and lips He said that his work mates had "put the pressure" on him, had called him a "wrong un" and a "copper's nark." He heard a voice in his head repeating "He is insane, he is insane" and other derogatory remarks He said he had been forced to protect himself and on one occasion had attacked a work-fellow with a knife He had also been drinking heavily for some months He was full of remorse for his wrong doings and felt that he was unworthy of his family

Response to E C T was good, and he left hospital and returned to work after eight weeks, but he soon began to drink again, and later became depressed and was readmitted, having been home for six months after a second suicidal attempt Further courses of E C T produced only temporary improvement, and he remained in hospital in a depressed and deluded state Orbital undercutting was performed three years after his original admission, and at this time he had been continually depressed for a year

Progress After Operation—After operation tension was still present at times, but he was not depressed. During the two postoperative months before his return home he gradually lost his tension, and was happy and friendly with the other patients whom he had previously believed were talking about him

Follow up—Four months after operation he remained well and entirely free from psychotic symptoms, depression, and tension and appeared placid and contented He looked after himself well spontaneously, occupied himself with jobs about the house, reading, and going for walks Immediately on discharge he was eager to start work again He was advised to take it easy for a while, but there is no doubt that he is now fit to do a full day's work

Discussion

Scoville (1949), who devised the first undercutting operations as opposed to topectomies and gyrectomies, suggested three sites for the operation according to the nature of the disorder (1) the superior convexity of the frontal cortex corresponding to Brodmann's areas 9 and 10; (2) the medial frontal cortex cingulate area, and (3) the orbital cortex areas 11 and 13 Scoville regarded the undercutting of the orbital cortex as the ideal operation for the relief of chronic neuroses and milder mood disturbances, because of the almost complete absence of personality changes Our best results are in just these conditions—i e, chronic anxiety states and chronic depressions—but some of the patients with a paranoid psychosis who had much tension or suspiciousness benefited greatly from the operation On the other hand, in severe psychotics the operation may be found insufficient quantitatively As mentioned above, case 5, in category B, had subsequently to undergo a standard leucotomy

In such an unpredictable field as neuro anatomy, especially in the present state of our knowledge, a discussion on correlation between clinical findings and operative lesions, examined post mortem, is not likely to be very profitable Much more material from recorded cases will have to be examined It may be of interest, however, to note that, according to Fulton (1951), the hypothalamus projects to the cerebral cortex by way of two main groups of thalamic nuclei, the anterior and the dorsomedial nuclei As regards the dorsomedial nucleus, the most medial portion is that which receives messages from the hypothalamus, and this projects to the orbital surface, especially the anterior part and the frontal pole (Le Gros Clark 1948, Le Gros Clark and Meyer 1950) The lateral part of the dorsomedial nucleus sends fibres to the convexity of the frontal lobe Neuro physiologists suggest that this tract provides an essential relay mechanism through which the activities of the hypothalamus can immediately influence those of the higher functional levels of the cerebral cortex Interruption of the pathway between the magnacellular portion of the dorsomedial nucleus and the orbital cortex may diminish to a very large extent the number of impulses influencing "consciousness," and in this way, it has been argued, provide relief from a state of tension

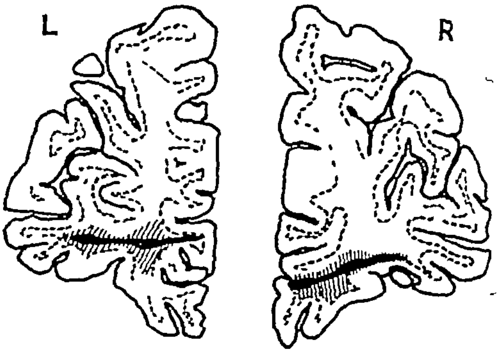
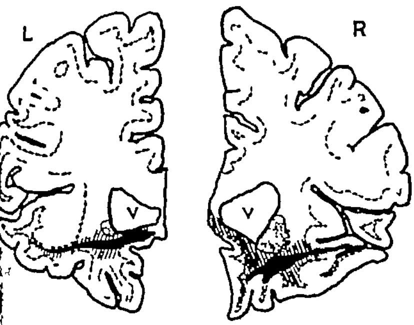


Fig 4—Coronal section 3 cm posterior to frontal pole (case 17): black, complete loss of tissue, hatched, partial loss of tissue (Traced from myelin-stained section)

In this connection the following neuro anatomical observations are of importance Patient 17, in category B, a woman of 26 with long standing paranoid schizophrenia and much deterioration, who was operated on in October, 1951, died of intercurrent disease (carcinoma of the ovary) two and a half years later We are indebted to Dr Corsellis for the following report

"*At the frontal pole on both sides there* was a horizontal slit-shaped cavity 2 0 cm × 3 0 mm, which first penetrated the polar cortex and then opened out into the white matter deep to the orbital surface On both sides, at a coronal level 3 0 cm. behind the frontal pole (fig 4), the medial two-thirds of the orbital cortex had been undercut, although on the left



g 5—Coronal section 4 cm. posterior to frontal pole (case 17): V ventricle; black complete loss of tissue; hatched partial loss of tissue. (Tracing from myelin-stained section.)

e the lesion was slightly more dorsally placed The widest onal extent of the undercutting was at a level 4·0 cm from e pole (fig 5) when the entire width was affected Posterior this level the lesions rapidly narrowed and they died out ntral to the most anterior limits of the heads of the caudate clei—i.e., 5·0–5·5 cm. from the frontal pole (fig 6)

Histologically the cavities were encircled by a narrow e of demyelination always less than a few millimetres deep part from the entry wounds the frontal cortex was not preciably affected and the only other changes were ondary ones related to the primary lesions. These included ateral degeneration of a small segment of the internal psule and of the medial part of the dorsomedial nucleus of e thalamus.

Although this case, from a clinical point of view is a d example because the patient was already grossly teriorated when operated on the neuro anatomical anges are of great interest because they seem to confirm at at least part of the tracts carrying visceral impulses m the hypothalamus via the thalamus had been ered The results of a more detailed investigation of e brain by Dr Corsellis will appear elsewhere No hard l fast conclusion can of course, be drawn from this le specimen; but continued study along these lines specimens become available will further our progress ards a more definitive method of relieving mental order by operation

Summary

The results in 27 patients who have undergone bilateral dercutting of the orbital cortex are described

The patients were divided clinically into two groups: with well preserved personalities, of whom 7 were onic neurotics (category A) and 14 who were deteriorated psychotics (category B) In category A 9 patients were afterwards discharged, of whom 7 were regarded as recovered and 2 as improved In category B 4 patients were discharged, of whom 1 was a social recovery 2 were improved and 1 was not improved

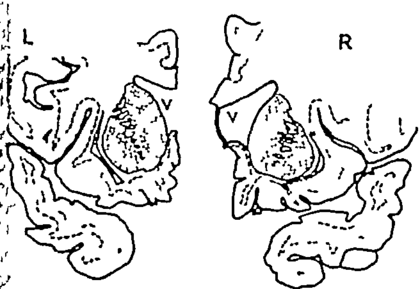
Of the remaining 3 in category A 2 improved in category B 5 did not improve and 1 of these subsequently underwent a standard leucotomy

There was no immediate postoperative death, but 1 patient with an abnormally small brain, in whom the cut had been carried too posteriorly died from extensive trophic ulceration five and a half months after operation

The *postoperative personality* changes have been negligible or very slight and have never reached the disturbing proportions seen after standard or medial leucotomy

The absence of serious personality defects and other complications after undercutting of the orbital cortex renders this operation preferable to standard leucotomy in chronic and apparently intractable neurosis or depression

This operation is also to be recommended in well preserved psychotics who exhibit tension and psychomotor unrest due to delusions and hallucinations



g 6—Coronal section 5 cm. posterior to frontal pole (case 17): V ventricle. (Tracing from myelin-stained section.)

Our thanks are due to Dr J A. N Corsellis, neuropathologist to Runwell Hospital for neuropathological reports and to Dr Graham Foulds, senior psychologist to the hospital, for psychological investigations We are also greatly indebted to Dr S Wiseberg registrar at the hospital for assistance in the preparation of case histories and follow up interviews

REFERENCES

Clark W E Le G (1948) *Lancet*, i, 353
— Meyer M. (1950) *Brit med Bull* 6 341
Fulton, J F (1951) Frontal Lobotomy and Affective Behaviour London p 44
McLardy T (1950) *J Neurol Psychiat* 13 106
Rylander G Personal Communication quoted by Fulton (1951) p 134
Scoville, W B (1949) *J Neurosurg* 6, 65
Strom Olsen R. (1946) *Proc R Soc Med* 39 431
— Tow P M. (1949) *Lancet*, i 87
Tow P M Lewin, W (1953) *Ibid* ii, 644

THRUSH ŒSOPHAGITIS WITH PHARYNGEAL INCOÖRDINATION

TREATED WITH HYDROXYSTILBAMIDINE

O H. WOLFF
M.D Camb., M.R C P
LECTURER IN PÆDIATRICS AND CHILD HEALTH UNIVERSITY OF BIRMINGHAM

B W PETTY
M B Birm., D Obst.
RESIDENT MEDICAL OFFICER, THE CHILDREN'S HOSPITAL, BIRMINGHAM

R ASTLEY
M.B Birm., D.M R
CONSULTANT RADIOLOGIST THE CHILDREN'S HOSPITAL

J M. SMELLIE
O B.E., T D M D Edin., F R.C P
PROFESSOR OF PÆDIATRICS AND CHILD HEALTH IN THE UNIVERSITY OF BIRMINGHAM

This report describes thrush œsophagitis in two new born infants in whom a disorder of swallowing led to aspiration pneumonia Treatment with hydroxystilbamidine not previously used in this condition was effective.

Case reports

Case 1—A girl aged 17 days and weighing 6 lb 6 oz (birth weight 6 lb) was admitted on July 24 1954 with a 24 hour history of vomiting and refusal of feeds.

Her general condition was fair A white membrane from which *Candida albicans* was isolated covered the tongue and buccal mucous membrane The vomiting and refusal of feeds suggested spread of the thrush to the œsophagus Treatment with gentian violet (1% paint to the mouth, and 0 01% 4 ml three times daily to swallow) was started

During the next 3 days reluctance to feed and occasional vomiting persisted, and her general condition remained unchanged Then, on July 28, she developed bronchopneumonia, confirmed by radiography Despite a course of sulphadimidine her condition deteriorated further during the next 48 hours The oral thrush persisted, and a profuse viscid discharge now poured from nose and mouth On July 30 a course of penicillin, previously avoided because of the thrush, was started, but the downhill course continued, and it seemed that the infant had not much longer to live At this stage vomiting, inability to swallow either food or the secretions from the nose and mouth, and repeated attacks of cyanosis despite oxygen therapy were the outstanding features The pulse rate was 180 and respirations were 80 per min Feeds had to be given by œsophageal tube passed through the mouth, because the nostrils were blocked by œdema and secretions Frequent sucking out of the nose, mouth, and pharynx was necessary to save the infant from suffocation On July 31 the house physician noted in the case records "I fear the worst"

On Aug 1 sulphadimidine, penicillin, gentian violet, and œsophageal feeds were discontinued, and an intravenous infusion was started At 10 P M the first dose of hydroxystilbamidine was given 15 mg (5 mg per kg body weight) dissolved in 0 75 ml of water was injected slowly into the rubber tubing above the drip chamber This dose was repeated 12-hourly Next morning she had improved remarkably, her respiration was slower (64 per min) and less laboured, and her pulse rate had fallen to 140 That night, however, she had a further attack of cyanosis This led us to start a course of streptomycin in addition to the hydroxystilbamidine, because it was impossible to decide whether there was a true thrush pneumonia or a bacterial aspiration pneumonia secondary to the thrush œsophagitis and stomatitis The latter diagnosis was supported in retrospect by the isolation of a coagulase positive *Staphylococcus aureus*, sensitive to streptomycin but insensitive to penicillin, from a blood culture taken on Aug 1

During the next week the baby improved steadily The nasal discharge and obstruction cleared within 24 hours of starting treatment with hydroxystilbamidine, the oral thrush membrane disappeared rapidly, no further *C albicans* was isolated, and radiography on Aug 6 showed decreased pulmonary involvement Because of this improvement and also because signs of thrombophlebitis had appeared, intravenous fluids and hydroxystilbamidine were stopped after a 6 day course, and oral feeds were begun again She took small amounts well, but, as the feeds were increased, she again started to cough and splutter, and on Aug 8 she had an attack of cyanosis On Aug 11 fluoroscopy showed bilateral basal collapse as well as incoördination of swallowing, which caused much iodised oil to enter the tracheobronchial tree Œsophageal feeding was recommenced and again she improved, though fluoroscopy on Aug 20 showed persistence of the incoördination

On Aug 26 feeding by teat was attempted once more, and this time there was no spluttering or choking Further progress was very satisfactory The baby was discharged on Sept 19, and when she was last seen on Nov 22 her condition was excellent, she had gained 4 lb and a chest radiograph was normal

Case 2 —A boy, aged 24 hours, was admitted on Oct 19, 1954 Pregnancy and delivery normal Birth weight 7 lb A few hours after birth a generalised petechial rash had appeared.

His condition was good, and there were no other abnormal signs A blood-count showed 56,000 platelets per c mm and 6000 leucocytes (1140 polymorphs) per c mm The discovery of thrombagglutinins (Stefanini and Dameshek 1953) and leukagglutinins (Dausset et al 1954) in the sera of the infant and of his mother explained the purpura and granulocytopenia

No fresh petechiæ appeared after admission, although the platelet-count on Oct 23 was only 32,000 per c.mm On Oct 25, however, he had purulent conjunctivitis of the right eye, omphalitis, septic blisters on the face, and oral thrush Oral and conjunctival swabs grew *C albicans* A *Staph aureus*, sensitive to aureomycin but insensitive to penicillin, was also isolated from the conjunctiva The septic skin lesions, conjunctivitis, and omphalitis cleared rapidly with a 6-day course of aureomycin 20 mg 6 hourly The thrush stomatitis was t[illegible] gentian violet paint Occasional vomiting suggested spread of the thrush to the œsophagus, so the baby was also given gentian-violet to swallow

Even after aureomycin had been discontinued on Nov 1, the thrush spread further until the tongue and oral mucosa were completely covered, and on Nov 2 *C albicans* was isolated from stomach washings A blood count on Nov 3 showed 7400 polymorphs per c.mm but still only 135,000 platelets per c mm His condition gradually deteriorated

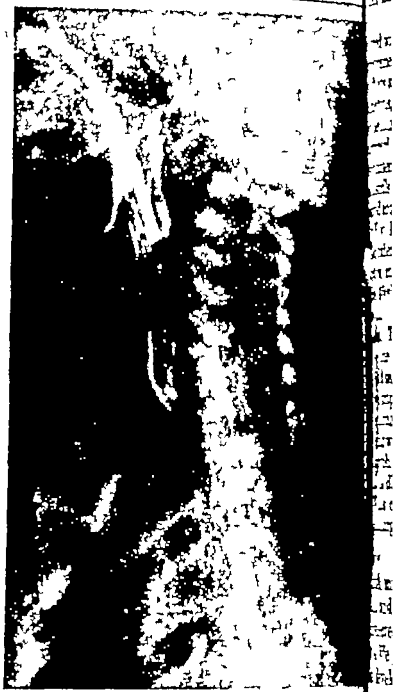


Fig 1—Case 2 Incoördinated swallowing oil has passed into nasopharynx and trach

He became reluctant to take feeds, milk was retained in mouth and dribbled from the corners, there was splutter and he had several attacks of cyanosis It was often nece to suck out his nose, mouth, and pharynx, where much mucus accumulated and interfered with breathing

On Nov 4 one of us (R A) examined the infant fl scopically the contrast medium was held in the mouth rejected, very little was swallowed If contrast me was injected into the back of the mouth or pharynx, swall was seen to be incoördinated Iodised oil passed up int nasal cavity and down the trachea, little entered the phagus (fig 1) If oil was injected directly into the œsoph it passed down reasonably well The picture was th pharyngeal incoördination of swallowing The lungs were

During the next 24 hours his condition deteriorated fu The temperature rose to 101 6°F, the pulse rate to 18 the respirations to 90 per min

On Nov 5 local treatment to the mouth was disconti and intravenous fluids were substituted for oral feeds S taneou treatment hydroxy bamidin mg 12 ho was start being give the sa method as case 1 Th improveme during th next 2 da was remark able Afte hours trea ment wit hydroxys bamidin cultures fr oral swabs stomac washings d not grow *albicans* Th oral membr started to p on Nov 7, by Nov 12 mouth

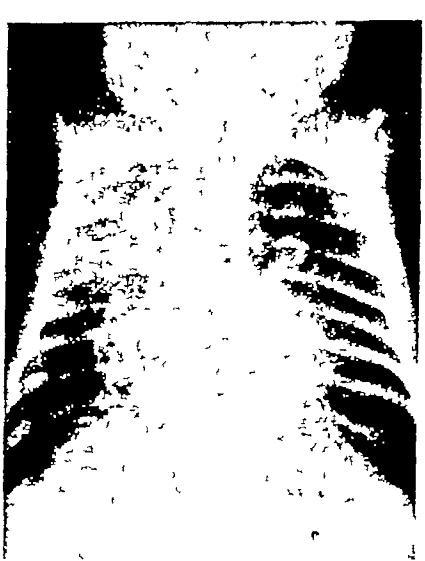


Fig 2—Case 2 : aspiration pneumonia.

vered with healthy looking mucosa. Because of this rapid provement, and also because the leg into which the intraven fluids and the drug had been given showed signs of throm phlebitis, hydroxystilbamidine was stopped on Nov 9 and l feeding restarted Within 24 hours all the symptoms of ryngeal incoördination recurred with reluctance to feed spluttering *Frequent suction of secretions from the mouth* nostrils was necessary Oral feeding had obviously been arted too soon.

On Nov 13 the baby developed pneumonia: a radiograph wed extensive consolidation in both lungs, consistent with ration into the bronchial tree (fig 2) A blood-count wed 4500 polymorphs per c.mm and 320 000 platelets r c.mm *Staph aureus* was isolated from oral and nasal retions. Treatment with streptomycin and erythromycin, which the organism was sensitive was started The infant nursed in oxygen and tube fed. After an anxious few days gain improved and fluoroscopy on Nov 22 showed a mal though rather slow swallowing reflex. Consequently al feeding was restarted and further progress was uneventful. radiograph on Dec 8 showed resolution of the consolidation, d he was discharged on Dec 11 When he was last seen on c. 22 his condition was excellent and he had gained 2lb e discharge.

Discussion

cidence

Thrush infections are common during early infancy dlam and Henderson (1942) swabbed the mouths of unselected infants at intervals during the first ten ys of life they isolated *C albicans* from 11 all of om developed clinical thrush a further 3 infants, king a total of 23% developed thrush before leaving pital. Anderson et al (1944) found an incidence of 7% of clinical thrush in newborn infants and like dlam and Henderson noted that, whenever *C albicans* s cultured thrush developed in two or three days. e use of antibiotics has made thrush infections even re frequent (Amhe 1952 Holzel 1953 Nikolowski 1953) commonly these infections are mild remain localised the mouth or skin and respond readily to gentian let or to borax in glycerin Probably such mild cases en remain undiagnosed and recover spontaneously t infrequently however the infection takes a less lign course spreads beyond the mouth into the rynx oesophagus larynx, and bronchi or rarely into lungs or blood-stream, and may kill the infant

bbs (1938) at the Children s Hospital, Birmingham found ng a three-year period 23 instances of thrush oesophagitis cropsies on infants. He regarded the thrush as the cause ath and not as a terminal complication of some other dition. Ludlam and Henderson (1942) over a four year d found 20 cases of thrush oesophagitis at necropsy The nce in infants who died after forty eight hours of life 6 6%. The thrush appeared to be the cause of death in cases. In another series, of 2, 10 infants who survived for e than forty-eight hours the same observers found 163 of thrush. 20 of these died from various causes necropsy done in 18; in 8 the thrush had spread to the pharynx l in 7 of these it had also invaded the oesophagus In 2 es it had spread to the stomach Lederer and Todd (1949) nd either pharyngeal or oesophageal thrush in 7 of 28 opsies on newborn babies and in 10 of 170 necropsies on ants 1–12 months old

Whereas the diagnosis of oral thrush is usually easy in thrush in early infancy is often unrecognised par ularly when it occurs without oral thrush The atest difficulties however arise in the diagnosis of ush involving the pharynx oesophagus, larynx or respiratory tract below the larynx The *British dical Journal* (1950) stated that the diagnosis of [illegible] thrush is a matter of conjecture and can nerally be made with certainty only after death derer and Todd (1949) thought that the diagnostic ficulties in the living and even at necropsy might be ponsible for fatal thrush lesions remaining undetected d unrecorded In the presence of oral lesions a deteri ation in an infant s condition will suggest extension of e thrush; but pharyngeal lesions may occur in the sence of or with only inconspicuous oral thrush

Clinical Features

In view of the difficulty of exact definition of the extent of the thrush infection, we shall for convenience refer to the syndrome as "thrush oesophagitis," realising that the pharynx and respiratory tract may also be involved Ebbs (1938) Ludlam and Henderson (1942) Adams (1944) and Lederer and Todd (1949) described the clinical features of this syndrome Their descriptions agree closely with each other and with the findings in our cases

Initially there is crying during feeds and regurgitation or vomiting, which is occasionally projectile, the vomit may contain blood. Then feeds are refused or retained in the mouth and dribble from its corners, much thick mucus accumulates in the mouth and nose Despite correction of dehydration an intense toxæmia develops often with a subnormal temperature During feeds attacks of cyanosis occur which Ebbs (1938) ascribed to aspiration of vomit Lederer and Todd (1949), however postulated pharyngeal incoördination leading to direct entry of milk into the respiratory tract. This hypothesis we have been able to prove by fluoroscopy and by ciné-radiography by the technique described by Astley (1955),

In both children there was a disorder of deglutition largely restricted to the pharynx transit through the oesophagus was relatively normal and only hindered by respiratory distress. Much of the opaque medium remained in the pharynx for some seconds contrasting strongly with the normal rapid passage The pharyngeal space remained open and its communicating passages patent; the larynx did not rise and the nasal cavity was not closed off by the soft palate In consequence iodised oil passed upwards into the nose and downwards into the larynx and tracheobronchial tree During much of the time the epiglottis remained erect amidst the contrast medium There was not however an absolute paralysis; occasionally the larynx rose and the pharyngeal space was obliterated Infrequently a bolus passed much more normally and the epiglottis turned down with it in the usual manner (Ardran and Kemp 1952)

These findings suggest that the pneumonia, which has been regarded by previous writers as such a constant terminal event (Ebbs 1938 Ludlam and Henderson 1942 Glanzmann and Riniker 1950) is at least sometimes due to a complicating disorder of swallowing A true thrush pneumonia is probably rare (Adams 1944 *British Medical Journal* 1950) the causal organisms usually being secondary pyogenic invaders, particularly *Staph. aureus* (Ludlam and Henderson 1942, Adams 1944, Lederer and Todd 1949, Glanzmann and Riniker 1950, Amhe 1952)

Treatment with Hydroxystilbamidine

Hydroxystilbamidine is one of the series of aromatic diamidine compounds synthesised by Ashley and Harris (1946) in the laboratories of Messrs May & Baker Fulton (1944a) found it of prophylactic value against *Trypanosoma rhodesiense* inoculations in mice In *Leishmania donovani* infections in golden hamsters it was as effective as stilbamidine (Fulton 1944b) Hydroxystilbamidine has been used in the treatment of multiple myeloma (Snapper 1948) kala azar (Sen Gupta 1949) mucocutaneous leishmaniasis (Snapper 1952) blastomycosis (Snapper and McVay 1953, Smith 1953 Colsky 1954 Sutliff et al 1954 Weinberg et al. 1954) and a coccidioidal infection involving a single bone (Grebe 1954) Trigeminal neuropathy, which is a relatively frequent and distressing complication of stilbamidine treatment (Napier and Sen Gupta 1942 Collard and Hargreaves 1947, Schoenbach and Greenspan 1948) and led Snapper et al (1952) and Curtis et al (1954) to abandon its use has not been reported after treatment with hydroxystilbamidine

We have not found an account of thrush infections in man treated with stilbamidine or hydroxystilbamidine A trial of these compounds was suggested by their success in other mycotic infections Solotorovsky et al (1954) showed that stilbamidine and hydroxystilbamidine are moderately active against *C albicans* in vitro but inactive in mice However, failure of a drug to cure fungus infections in mice does not necessarily imply failure in man For example, Schwarz and Adriano (1953) failed to arrest experimental blastomycosis in mice with stilbamidine, yet in human infections its value is beyond doubt Schoenbach and Greenspan (1948), in their excellent review of the aromatic diamidines, state that the host drug relationship is as important as the host parasite and parasite drug relationships Smith (1953) and Snapper and McVay (1953) expressed similar views

The pharmacology of hydroxystilbamidine has been reviewed by Snapper et al (1952) and Smith (1953) The following brief account is largely based on these reviews and that of Schoenbach and Greenspan (1948), which deals with the aromatic diamidines in general

Hydroxystilbamidine is 4 4′ diamidino 2 hydroxystilbene The compound used in our cases was 4 4′ diamidino 2-hydroxystilbene di β hydroxyethanesulphonate, which contains 54% of base For brevity we have used the term hydroxystilbamidine in place of the full chemical name of its salt After an intravenous dose of 2 mg of stilbamidine or hydroxystilbamidine per kg body weight only about 15% is excreted in the urine in twenty four hours After daily doses for seven or eight days the amount excreted in the urine increases progressively to a maximum of 70–80% in twenty-four hours, this suggests that the body proteins gradually become saturated with the diamidines, after which the excess is largely excreted in the urine It is likely that the remarkable adsorptive qualities of the diamidines account for the progressive improvement which may take place long after cessation of therapy *Snapper et al (1951) found traces of diamidines in the body three years after administration*

Administration—Sen Gupta (1949) and Grebe (1954) observed that hydroxystilbamidine given intramuscularly caused pain at the site of injection, Smith (1953) condemned the intramuscular route for the same reason and as a possible cause of local necrosis The intravenous route appears preferable, though Snapper and McVay (1953) noted little pain or tissue reaction after intramuscular injection with procaine (75 mg of hydroxystilbamidine in 2 ml of 5% glucose in physiological saline solution containing 20 mg of procaine) Snapper (1948) and Sen Gupta (1949) dissolved hydroxystilbamidine in 10 ml of water and 25 ml of 25% glucose respectively and injected it slowly into a vein Snapper (1952), Smith (1953), Colsky (1954), Grebe (1954), and Weinberg et al (1954) gave 225 mg daily (the dose for adults) dissolved in 200–300 ml of 5% dextrose or of saline solution by continuous intravenous drip over periods ranging from half an hour to three hours Continuous drip is probably preferable to intravenous injection, which may be followed by thrombophlebitis After rapid injection transient pallor, dizziness, a fall in blood pressure, and tachycardia have been reported (Schoenbach and Greenspan 1948, Smith 1953)

Published reports deal mainly with adults, and we have been unable to find an account of hydroxystilbamidine used in infants At this age daily intravenous injections are difficult to give In our two cases we discontinued oral feeds, administered fluids by continuous intravenous drip, and injected the hydroxystilbamidine (15 mg in 0 75 ml of water) slowly into the rubber tubing above the drip chamber The occurrence in both infants of venous spasm after injection, and later of thrombophlebitis, suggests that it might be better to give the compound by continuous drip over two or three hours

Smith (1953) noted that a precipitate forms when concentrations greater than 0 5% of stilbamidine are added to human serum, and suggested that this may explain the occasional immediate toxic effects after intravenous injection of concentrated solutions We also noticed a precipitate in the drip chamber when hydroxystilbamidine was injected into the rubber tubing while plas[illegible] being infused, though our infants showed [illegible] toxic effects After this observation the hydroxystilbamidine was injected into glucose and saline solutions, with which no precipitate formed

Dose—The dose commonly recommended for adul 3–5 mg per kg body weight daily or on alternate da As infants usually require relatively greater amount chemotherapeutic agents, we decided on a dose of 5 per kg, and the infants' very poor condition led us repeat the dose twelve hourly Treatment was contin for six and four days respectively (total doses 180 in case 1 and 120 mg in case 2) Because of the rate of excretion of hydroxystilbamidine, the rapid appearance of the thrush lesions, and the developme thrombophlebitis we decided against a longer cours treatment The optimum therapeutic régime will onl discovered after further trials of hydroxystilbamidi in severe thrush infections Our experience with the two cases has convinced us that such trials are just whenever the response to simpler remedies is uns factory, especially when the infection has spread be the skin or the mouth

Adjuvant Therapy

As secondary pyogenic invasion is important, it advisable in the more severe cases to use a potent bacterial agent in addition to hydroxystilbamidine in case 1, where streptomycin was given The disapp ance of the thrush membrane from the mouth must be taken as evidence that there can be a return to feeding, this mistake, which we made in both ca led to the development of pneumonia There wa latent period between the disappearance of the membr and the return of normal deglutition—an observatio not recorded previously, probably because before advent of hydroxystilbamidine no such seriously infant had survived It appears advisable to fo intravenous feeding, which is necessary at the heig the illness, by a period of tube feeding We sug that after the disappearance of the thrush memb *fluoroscopy should be employed to demonstrate* no *swallowing before oral feeds are restarted*

Summary

A severe thrush infection of the upper alimentar respiratory tracts may be accompanied by a c picture due to incoordination of swallowing

This incoördination may lead to pneumonia

Hydroxystilbamidine was an effective form of tr ment in the two cases described

Secondary pyogenic invasion is an important comp tion requiring additional treatment

Disordered swallowing may persist for several after the disappearance of the thrush membrane fr the mouth, fluoroscopy is advisable before reco mencing oral feeding

We are indebted to Dr H S Baar for suggesting demonstrating the presence of leukagglutinins and thr agglutinins in case 2, and to Dr W R Thrower who first d our attention to the possible value of hydroxystilbamidi thrush and helped us with case 1 We gratefully acknow the invaluable nursing services of Sister J Woodward her staff Messrs May & Baker supplied the hydrox bamidine

Addendum

Since submitting this report for publication we have tre a third infant suffering from thrush œsophagitis incoord tion of swallowing, and aspiration pneumonia The c was 3 weeks old Hydroxystilbamidine was given d over two to three hours by continuous intravenous drip a scalp vein The compound was given twice daily for days No thrombophlebitis occurred and we were abl use the same vein throughout this period The baby m an excellent and rapid recovery

REFERENCES

Adams, J M (1944) *J Pediat* 25 309
Amlie R (1952) *Ann paediat* 179 316
Anderson N A Sage D N, Spaulding E H (1941) *Amer J D Child* 67, 450
Ardran, G M. Kemp, F H (1952) *Brit J Radiol* 25 406
Ashley, J N, Harris J O (1946) *J chem Soc* 2 567

References continued at foot of next column

THE USE OF ACETAZOLEAMIDE IN ACUTE RESPIRATORY ACIDOSIS

MARY WISHART
B.Sc., M.B Glasg
HOUSE PHYSICIAN

BERNARD ISAACS
M.B Glasg F.R.F.P.S D Obst
REGISTRAR

STOBHILL GENERAL HOSPITAL, GLASGOW

The heterocyclic sulphonamide 2 acetylamino 1 3 4 thiadiazole-5-sulphonamide (acetazoleamide Diamox, Lederle), inhibits the enzyme carbonic anhydrase, its main pharmacological effect being exerted on the renal tubule cells (Miller et al 1950 Berliner et al 1951) leading to increased urinary excretion of sodium potassium, and bicarbonate reduced excretion of ammonium ion, a rise in pH of the urine and a fall in the serum-bicarbonate level and in pH of the blood (Nadell 1953 Counihan et al. 1954)

The treatment of respiratory acidosis with acetazoleamide was suggested by Nadell (1953) who obtained favourable results in 6 cases Similar results were obtained by Heiskell et al (1954) in 4 ambulant patients with pulmonary emphysema and by Ruskin (1955) in a case of cor pulmonale

The rationale of this therapy was elaborated by Nadell (1953). She found in 2 controls and in 5 of 6 patients with respiratory acidosis that when acetazoleamide was first given both the serum bicarbonate level and the pH of the serum fell with continued therapy the pH returned to normal but the serum bicarbonate level remained low This must have been due to a fall in the partial pressure of carbon dioxide in the blood (pCO_2) produced by respiratory compensation for the metabolic acidosis. Nadell commented that pulmonary dissipation of carbon dioxide seemed to be more effective after the administration of acetazoleamide but the mechanism is obscure

Some criticism of this argument might be advanced In respiratory acidosis the respiratory centre is already relatively insensitive to the stimulus of a high pCO_2 the ventilatory function of the lungs is so impaired that alveolar loss of carbon dioxide cannot be significantly increased despite additional stimulation of the respiratory centre (Wilson et al. 1954 Cohn et al 1954) and urinary loss of bicarbonate in response to the administration of acetazoleamide would tend to alter the ratio of serum bicarbonate to pCO_2, with a fall in pH which is potentially harmful to a patient who is already acidotic

Despite these theoretical objections we have given acetazoleamide to 3 patients with acute respiratory acidosis in the hope of preventing or relieving carbon dioxide narcosis. The patients all had chronic bronchitis emphysema and pulmonary heart-disease and their symptoms had been severely aggravated by acute respiratory infection. Striking biochemical changes took place in all the patients after the administration of acetazoleamide but no clinical improvement was noted Judged clinically the condition of the 1st patient was deteriorating before acetazoleamide was given the drug did not influence the course of the disease and the patient died In the 2nd patient the administration of acetazoleamide was immediately followed by much clinical deterioration a rapid downhill course ending in death The 3rd patient showed an alarming deterioration of the clinical condition after a single dose of acetazoleamide but improved when the drug was withheld

Case reports

Case 1 —A woman aged 59 was admitted to hospital with a severe acute respiratory infection She had chronic bronchitis of five years duration, and this was now accompanied by emphysema and pulmonary heart-disease On admission she was pyrexial, dyspnœic and cyanosed but conscious and rational.

Treatment and Course—She was treated with penicillin digitalis, and mersalyl and oxygen was given in small amount by nasal catheter with relief of cyanosis. Next day her general condition gradually deteriorated and she became comatose Her optic fundi showed gross distension and tortuosity of veins and congestion of the optic discs. Her serum bicarbonate level was 37 8 m.eq per litre and her serum urea level was raised but her serum potassium level was normal and remained so throughout the illness. She was given acetazoleamide 500 mg on the day after admission and the same dose was given daily for the next three days, and then every second day for three more doses. Eighteen hours after the first dose of acetazoleamide the serum bicarbonate level had fallen to 29 7 m.eq per litre but no clinical improvement was noted The serum bicarbonate level in the next ten days ranged from 32 4 to 41 8 m.eq per litre Oxygen therapy was continued by intermittent use of the oxygen tent and oxytetracycline was given The patient remained critically ill, with pyrexia dyspnœa and drowsiness, and four weeks after admission she lapsed into coma and died

Necropsy showed chronic bronchitis, emphysema recent bronchopneumonia right ventricular enlargement and congestive cardiac failure

Case 2 —A woman aged 63 with nine years history of chronic bronchitis, was admitted to hospital with an acute exacerbation of pulmonary heart disease following an infection of her upper respiratory tract On admission she was cyanosed and dyspnœic but conscious and rational

Treatment and Course—Penicillin and digitalis were administered but oxygen was at first withheld On the day after admission the serum bicarbonate level was 36 0 m.eq per litre The optic fundi showed dilatation and tortuosity of the veins, and the discs were slightly swollen. Oxygen therapy was started by nasal catheter and acetazoleamide 500 mg was given. Twenty four hours later the serum bicarbonate level had fallen to 32 4 m eq per litre and in that period the patient excreted 705 ml of urine containing 31 5 m.eq of bicarbonate On the second day after admission the patient became drowsy and confused and was placed in an oxygen tent She was given acetazoleamide 500 mg twice on that day and once more on the third day the serum bicarbonate level then having risen again to 30·0 m eq per litre The serum potassium level was normal Her condition rapidly deteriorated the drowsiness deepened into coma and she died on the third day after admission

Necropsy showed chronic bronchitis and
recent pneumonic lesion fatty infiltration of
and enlargement of the right ventricle
cerebral oedema but no local lesion in the

Case 3 —A woman aged 60 with
chronic bronchitis with emphysema a

DR. WOLFF AND OTHERS: REFERENCES—continued
y R. (1955) Brit J Radiol 28 ?41
Medical Journal (1950) ii, 1430
rd, P J., Hargreaves, W H (1947) Lancet ii 686
y J (1954) Arch. intern Med 93, 796
C. C. Bocobo F C, Harrell E. R Block W D (1954)
U.S Forces med J 5 919
J Nenna A, Berry H (1954) Blood 9 696
J H (1938) Arch Dis. Childh 13 211
J D (1941a) Ann trop Med Parasit 35 78
(1941b) Ibid p 147
mann, E., Hiniker, I (1950) Ann paediat 175 1
A (1954) J Bone Jt Surg, 36A, 850
A (1953) Arch Dis. Childh 28 412.
H., Todd R. M (1949) Ibid 24 ?00
O H, Henderson J L (1942) Lancet, i 64
L. E., Sen Gupta I C (1942) Indian med Gaz. 77 71
W (1953) Dtsch med Wschr 78 333
L. H., Greenspan, L. M (1948) Medicine Baltimore
27 327
J., Adriano S (1953) J. invest Derm 20 ?49
Gupta, I, C. (1938) Lancet ii, 97
D T (1953) GI (Kansas City Mo.) 8 69
I (1945) J Mt Sinai Hosp. 15 150
— (1952) Amer J Med 13 655
— Lieben, F., Greenspan E. Schneid B (1951) Cancer 4 1210
— McVay, L. V (1953) Amer J Med 15, 603
— Schneid B., McVay L., Lieben I (1954) Trans N Y Acad Sci 14 260
M., Imonson, E. J Gregory I J Winsten S (1954) Carmother 4 163
M., Dameshek, W (1953) Lancet ii ?09
W., D., Kyle J W Hobson J L. (1954) Ann. intern Med 41 88
H J., Lawrence C H., Buchholz, A (1954) Arch intern Med. 94 194

disease, was moderately ill when admitted for treatment of an acute respiratory infection.

Treatment and Progress—She improved under treatment with penicillin, digitalis, and oxygen given by nasal catheter Her serum bicarbonate level on admission was 49 5 m eq per litre, the level fell to 38 3 m eq per litre next day, but rose on the third day to 40 5 m eq per litre Acetazoleamide 500 mg was given on the third day In the next twenty four hours the patient excreted 1055 ml of urine containing 100 m.eq of bicarbonate, and the serum-bicarbonate level fell to 36 9 m eq per litre No more acetazoleamide was given, but renal excretion of bicarbonate continued for two more days, a further 62 m.eq of bicarbonate being excreted. This was accompanied by a further fall in serum bicarbonate level to 34 2 m eq per litre and 30 6 m eq per litre two and three days respectively after the administration of acetazoleamide Twenty four hours after the acetazoleamide had been given there was an unexpected serious deterioration in the patient's clinical condition respiration became shallow, cyanosis increased, and she became extremely drowsy She was placed in an oxygen tent, where she remained drowsy, confused, and breathless for two days, and then gradually improved During this time the physical signs in the chest were unchanged, the retinal veins were tortuous and congested, but there was no papillœdema, and the serum potassium level was normal Oxygen therapy was discontinued after three days, and the patient eventually made a good recovery The serum bicarbonate level was estimated every second day in the next week as 38 7, 32 0, and 37 8 m.eq per litre

Discussion

The clinical deterioration in these 3 patients depended on a combination of toxæmia, hypoxia, and retention of carbon dioxide Toxæmia played an important part in case 1, but in the 2 other patients the infection responded initially to treatment with an antibiotic Anoxia was present in all the patients, and our policy was to relieve this gradually, following the advice of Simpson (1954) by giving oxygen at first by nasal catheter at a rate of flow of 2–4 litres a minute, and only later transferring the patients to an oxygen tent Retention of carbon dioxide was probably a major factor leading to deterioration, and oxygen therapy may have contributed to this

In any attempt to measure the effects of retention of carbon dioxide the relevant physiological observations are the alveolar concentration of carbon dioxide and the pH of the serum, from which can be determined the pCO_2 It is unfortunate that it was impossible to obtain these measurements in our patients The serum bicarbonate level gave no indication of the clinical condition Case 2 was very much more ill, with an initial serum-bicarbonate level of 36 0 m eq per litre, than was case 3, whose serum-bicarbonate level on admission was 49 5 m eq per litre Considerable fluctuations in the serum-biocarbonate level in case 3 have already been noted, these were independent of treatment and unrelated to the clinical condition There seems to be no doubt, however, that acetazoleamide caused an initial fall in the serum-bicarbonate level in all 3 patients The lack of clinical improvement suggests that the fall of the serum-bicarbonate level was not accompanied by a corresponding fall in pCO_2, presumably because of pulmonary insufficiency We cannot offer direct proof of this hypothesis, but, if it is true, the initial effect of acetazoleamide in these patients was to alter the ratio of pCO_2 to serum-bicarbonate in such a way as to cause a potenti ally dangerous fall in serum pH There is ample evidence that this happens when acetazoleamide is administered to patients with normal respiratory function (e g, Nadell 1953, Counihan et al 1954), and Simpson has demonstrated that the same mechanism operated in his own cases of respiratory acidosis The rapid return of the serum bicarbonate level to its initial high value in cases 1 and 2 was not accompanied by improvement, possibly bec respiratory centre remained adversely affected by the persistently high pCO_2 or as a result of t temporary lowering of pH

We conclude that in these 3 cases of acute re acidosis accompanied by pulmonary infection aceta amide was of no value, and that its property of prom ing renal excretion of bicarbonate may have been har to the patients

Summary

The carbonic anhydrase inhibitor, acetazoleamide, given to 3 patients with acute exacerbation of respiratory acidosis

Increased urinary excretion of bicarbonate and of the serum bicarbonate level resulted

In all 3 cases there was clinical deterioration 2 patients died, and the 3rd recovered when the amide was withheld

It is concluded that acetazoleamide may be de in acute respiratory acidosis

We wish to thank Prof Stanley Alstead and Dr J Macarthur, under whose care these patients were treated, their advice and encouragement, and Dr J W and Dr A W Mollison for the biochemical estimations.

REFERENCES

Berliner, R W, Kennedy, T J jun, Orloff, J (1951) *Amer J* 11 274
Cohn, J E, Carroll D G, Riley, R. L (1954) *Ibid* 17, 44
Counihan, T B, Evans, B M., Milne, M D (1954) *Clin Sci*, 1
Heiskell, C L jun Belsky, J B, Klaumann, B F (1954) *J med Ass* 156 1059
Miller, W H, Dessert, A M, Roblin, R O jun (1950) *J chem Soc* 72 4893
Nadell J (1953) *J clin Invest* 32, 622
Ruskin, A (1955) *Arch intern Med* 95 24
Simpson, T (1954) *Brit med J* 1, 297
Wilson, R H, Hoseth, W, Dempsey, M. E (1954) *Amer J* 17, 464

TUBERCULIN AND LEPROMIN SENSITIVITY IN THE SOUTH AFRIC BANTU

A PILOT SURVEY

S W A Kuper
M B Rand, D P H., D T M & H, D C.P
CLINICAL PATHOLOGIST, BROMPTON HOSPITAL, LOND

It has often been stated that skin sensitivit tuberculin and lepromin are correlated, and it has inferred that this reflects an immunological relatio (Chaussinand 1950, Fernandez 1943, Lowe and Mc 1953b)

The significance of skin sensitivity to lepromin i clearly established, and this sensitivity is used as an to classification and prognosis in leprosy rather tha a means of diagnosis Most patients with leproma leprosy are relatively insensitive to lepromin, whe those with tuberculoid leprosy are said to show a marked allergic response, which may be either a "tu culin like" reaction at forty-eight to seventy two h (the Fernandez test) or an indurated nodule from tw five weeks after the inoculation The two types of r tion are said to parallel one another in the individ case (Fernandez 1940, Lowe and McNulty 1953b), but method of preparation of the antigen determines whe the early or the late reaction is the greater Much of published material on this subject is largely speculati but a good deal of the data appears to support the th that the degree of correspondence between tuberc and lepromin reactions is far greater than could accounted for if the two forms of sensitivity were co pletely unrelated

I describe here an attempt to elucidate some of the problems by tests on South African Bantu patients controls Patients with pulmonary tuberculosis others with leprosy were investigated together wi apparently healthy adults The numbers tested were

TABLE I—MEAN SIZES OF REACTIONS

Group	No of persons	Mean transverse diameter of reaction (standard error of mean)					
		Tuberculin at 48 hr	Nil reactors	Lepromin at 48 hr	Nil reactors	Lepromin at 4 weeks	Nil reactors
ntrols (adult males)	105	12·5 mm. (*0·48*)	6	3·6 mm (*0·34*)	8	3·7 mm. (*0·16*)	1
berculosis (adult males)	53	14·1 mm (*0·79*)	1	7·4 mm (*0·77*)	2	3·9 mm (*0·30*)	1
promatous leprosy (adult males)	33	16·6 mm (*3·18*)	1	3·4 mm (*0·53*)		1·6 mm. (*0·34*)	13
romatous leprosy (adult females)	15	21·0 mm (*6·63*)	1	2·5 mm (*0·31*)		0·7 mm (*0·19*)	7
berculoid leprosy (adult males)	25	10·6 mm (*1·14*)	3	15·0 mm (*1·41*)		7·2 mm (*1·19*)	2
berculoid leprosy (adult females)	12	5·0 mm (*1·23*)	2	8·8 mm (*1·60*)		5·8 mm. (*1·31*)	1
berculoid leprosy (male children)	7	6·0 mm (*3·20*)	3	11·6 mm (*3·56*)		5·4 mm (*2·11*)	2
berculoid leprosy (female children)	6	3·2 mm (*1·44*)	2	10·2 mm. (*3·12*)		6·2 mm (*2·36*)	

This table represents the mean transverse diameters of reactions recorded in all the groups of patients It lists the reactions to tuberlin at 48 hours, and to lepromin at 48 hours and at 4 weeks The standard error of the mean is included in parentheses after each result numbers of subjects in whom no reaction was found are given in a separate column, but they are included in the figures of totals for h group

ps but it was hoped that this disadvantage would be ercome by careful standardisation of methods (Guld d Rud 1953 Meyer et al 1951)

Methods

The persons tested were divided into three categories

Group 1—Patients with pulmonary tuberculosis (57 adult ales)

Group 2—Patients with leprosy (102 mostly adults but me children aged 10–16 years)

Group 3— *Controls* (*114 adult males*)

The patients with tuberculosis were in hospital during e trial. They showed no obvious evidence of leprosy adiographs of the chest were characteristic of pulmon y tuberculosis and tubercle bacilli had been isolated m the sputum in about 90% of the cases

The leprosy patients were all being treated in an stitution during the trial, and radiological examination thin the preceding few months showed no evidence of lmonary tuberculosis The clinical diagnosis of leprosy d in all cases been substantiated by examination of ne smears and the type of leprosy was classified by e experienced permanent medical staff of the institute sts were made in 52 patients with lepromatous leprosy d 50 with tuberculoid leprosy

The controls consisted entirely of adult industrial ployees working in a soap factory and resident in the y Within a few weeks of the start of the trial they were diographed to exclude anyone with a shadow suggesting lmonary tuberculosis No obvious evidence of leprosy s seen in any member of the group

So far as is known none of the persons in any group d ever received B C G vaccine

chniques

Dried *lepromin* of the Dharmendra type was prepared by . N Figueredo of the Acworth Leprosy Home Bombay his antigen produces more prominent early reactions than layed ones, and is therefore more strictly comparable to berculin than is the Mitsuda type of antigen. The lepromin s finally suspended in half the recommended volume of line solution to reduce the volume of the intradermal injec on from 0·2 ml to 0·1 ml It was sealed in ampoules in eat Britain and was used within a month of the date of lling

Tuberculin was used in the form of purified protein rivative It was dissolved and diluted so that 0·1 ml ntained 5 tuberculin units. It was thought that this small se of tuberculin would detect only high specific degrees of nsitivity (Palmer and Bates 1952 Palmer 1953) Tablets re dissolved freshly for each session of inoculations.

Syringes were of the all glass tuberculin type All the ringes were new and each was used for only one inoculating ssion to prevent possible transference of antigen Only new edles were used and they were discarded at the end of each ssion. The syringes were examined for leakage and the iteria recommended by Guld and Rud (1953) for field trials were adopted 48 syringes were tested by their method but nly [illegible] satisfied their requirements. Fortunately it was found that a light smear of silicone oil applied to the barrol of the syringe reduced leakage to such a degree that 37 out of 48 syringes could be used Several intradermal inoculations of water made with these syringes in hospital staff produced no evidence of sensitivity to the silicone oil

Procedure

All the inoculations and readings of results were made by me to minimise individual variations of judgment (Meyer et al 1951) All the controls were inoculated on one day and all the patients with leprosy and tuberculosis on another The injections were made in the skin of the ventral surface of the forearm about half way between the wrist and elbow The volume inoculated was in all cases 0·1 ml administered intradermally so as to raise a distinct bleb in the skin Lepromin was injected into the left arm and tuberculin into the right each patient received the two inoculations within a few minutes

Because of skin pigmentation in the patients no attempt was made to delimit areas of erythema Measurements were made of the induration produced the edges of the areas were carefully defined, and the transverse diameters measured in millimetres with a transparent rule The site of inoculation of the tuberculin was examined after forty eight hours that of the lepromin inoculation was examined at forty eight hours, and after one two three, four five and six weeks

Results

Table I shows that the tuberculous and the control groups consisted entirely of adult males, but the leprosy patients included adults and children of both sexes. Distinct variations are apparent between males and females and adults and children so the results are recorded under separate headings In figs 1–3 the sexes and ages are not separated

The numbers of subjects vary slightly from table to table depending on the numbers available for measurement on the day in question The controls for example were 114 after forty eight hours but only 105 of these presented themselves for examination on the twenty eighth day

The results may be examined in one of two ways In the first place evidence may be sought of any correlation between skin sensitivities to lepromin and tuberculin This is best elicited statistically by the examination of product moment correlations but dot diagrams give an approximate picture of the relationships (*fig 1*) (The product moment correlation takes into account the sizes of reactions in each patient and may be regarded as a statistic summarising the degree of association exhibited in the dot diagrams) In this investigation no correlation between the two forms of sensitivity was found in 105 controls nor was there any evidence of association in the 85 adults with leprosy In the 53 patients with pulmonary tuberculosis, however a definite positive correlation was obtained (product moment correlation = 0·40 The chance of this being a random result is less

1000)* A small positive correlation was also found between the tuberculin reactions at forty-eight hours, and the lepromin reactions at twenty-eight days It is smaller than the forty-eight-hour correlation, and possibly merely residual from it The need for caution in assessing the importance of the observation is emphasised by the failure to find any correlation between the tuberculin and lepromin reactions in the other two test groups

The results may also be examined in another way If the suggestion is accurate that there are antigens common to the tubercle and leprosy bacilli, one might expect to find skin hypersensitivity in each of the two diseases, to the causal organism of the other, or to products derived from it Patients with tuberculosis might react strongly to lepromin injection, and patients with leprosy to tuberculin This could never be more than an approximation, however, for lepromin hypersensitivity is far less regular, even in leprosy, than is tuberculin sensitivity in tuberculosis

Skin reactions to lepromin (examined at forty-eight hours) were compared in healthy adults and in patients with pulmonary tuberculosis The latter were found to be significantly more sensitive to lepromin than the controls (mean for tuberculous patients 7 4 mm, and for controls 3 8 mm), and the same trend is evident in histograms (fig 3) †

Conversely, skin reactions to tuberculin were compared in healthy adults and in patients with leprosy The picture is rather complex Patients with tub leprosy appear to react less strongly to tuberculin th do the normal controls (fig 2) This difference is siderably reduced, however, if the male patients are compared with the controls, all of whom were ma The mean size of reactions in the male patients wi tuberculoid leprosy was 10 6 mm, and that in the norm controls 12 5 mm The difference is not significant Th female leprosy patients cannot properly be compar with the male controls In lepromatous leprosy th measurements are widely scattered, the mean reactio however, are significantly greater (males, mean=1 mm) despite the fact that 12 members of this gro showed no reactions at all to tuberculin (fig 2) Th was a very high degree of tuberculin sensitivity in so members of this group

Much of the published work on skin reactions in lepro records the observed reactions in terms of an arbitrar scale of "positive" and "negative" reactors. So

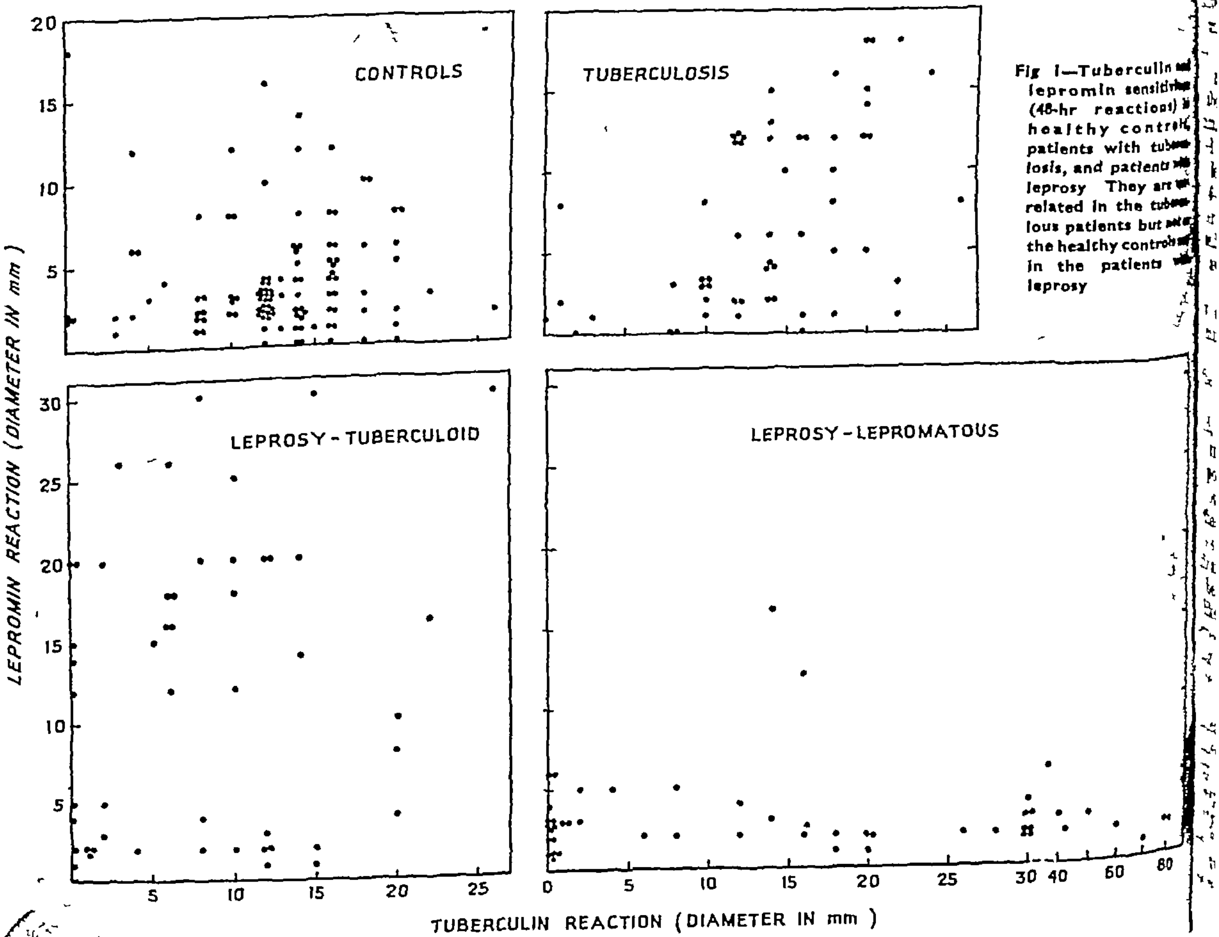


Fig 1—Tuberculin and lepromin sensitiv (48-hr reactions) healthy contr patients with tub losis, and patients leprosy They are related in the tub lous patients but the healthy contro in the patients leprosy

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* *Validity of Tests Used*—In comparing mean sizes of reactions *between the various groups, and in assessing the* significance of correlation between the reactions obtained to the two antigens, statistical tests were used which depend for their validity on the normal (gaussian) distribution of the measurements Evidently this type of distribution is not fulfilled, so the tests must be regarded as having only an approximate significance

† In figs 2 and 3 data relating to the forty eight hour tuberc and lepromin reactions are shown as histograms The gro intervals have been judiciously chosen to conceal th tendency towards recording even numbers of millimet *particularly in measuring* the relatively large reactio Superimposed on the histograms of the controls are th fitted logarithmic normal distributions, reached disregarding the information on reaction diameters than some arbitrarily selected level—8 mm in the c of tuberculin reactions, 1 5 mm in the case of lepro reactions (Hald 1952a and b)

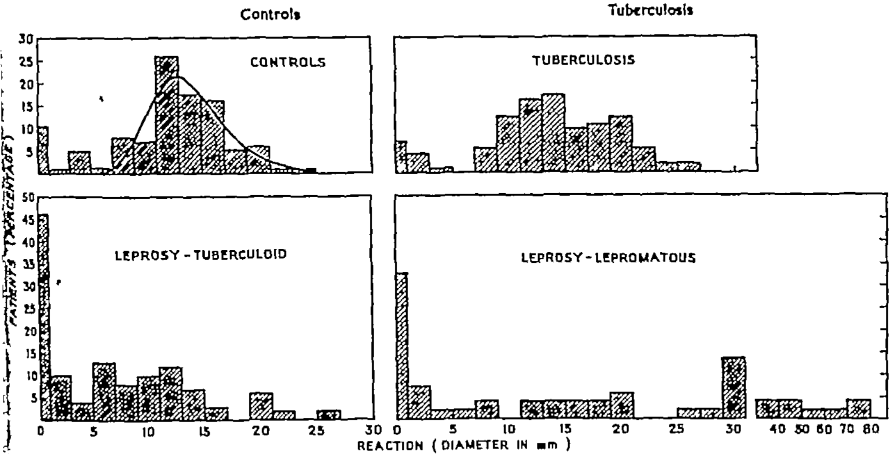

Fig 2—Tuberculin sensitivities (48-hr reactions) in healthy controls patients with tuberculosis and patients with leprosy

andards provide a useful rule of thumb for clinical urposes but their adoption in a survey of immunological actions leads to the discarding of a great deal of the formation (Edwards et al 1953) This trial records the tual observed measurements but it is possible to divide e readings at any desired level to facilitate comparison ith results published only in terms of 'positives' and negatives' Such comparison is obviously of limited lue unless conditions in the two surveys are very milar

Table II represents the results of this trial analysed the above lines Tuberculin reactions with a diameter 6 mm or more are corded as 'positive' lepromin reactions 0–10 mm. in ameter as 'doubtful' and 11 mm or ore as positive These criteria for rty eight hour promin reactions ere recommended y the International eprosy Congress in adrid 1953) In ble II 'doubtful' nd "positive" results re grouped together y this method of nalysis the results are gnificant only if it an be shown that e likelihood of the bserved distributions aving occurred by hance is less than 20 This level of gnificance was not ttained by any of the roups in this series.

Despite the possibility of errors in classification between the types of leprosy the results for the two groups are not 'combined' for any of the investigations This precaution was deemed necessary because of the widely divergent patterns of skin sensitivity in the two forms of leprosy It may be argued that the clinical classification was possibly biased by the results of earlier lepromin reactions but the pictures of tuberculin sensitivity in the two forms of leprosy are so widely different that it appears to reduce to a minimum the likelihood of widespread misclassification of the type of disease.

Early and Late Lepromin Reactions

The forty-eight-hour lepromin reaction is not significantly different in controls and in patients with lepro

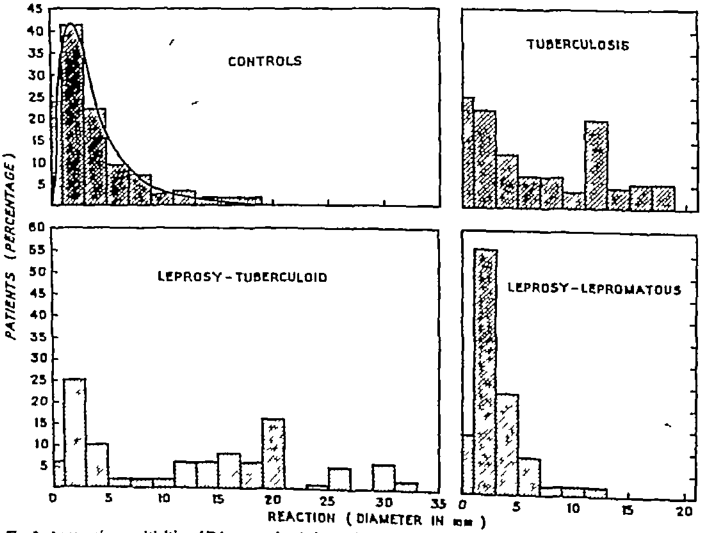

Fig. 3—Lepromin sensitivities (48-hr reactions) in healthy controls, patients with tuberculosis and patients with leprosy

TABLE II—NUMBERS OF "POSITIVE" AND "NEGATIVE" REACTORS

Group	Tuberculin negative (0–5 mm)		Tuberculin-positive (≥6 mm)		Total
	Lepromin negative (0–5 mm)	Lepromin positive or doubtful (≥6 mm)	Lepromin negative	Lepromin positive or doubtful	
Controls	8	4	80	22	114
Tuberculosis	4	1	24	28	57
Lepromatous leprosy (males)	12	1	17	3	33
Lepromatous leprosy (females)	6	2	11	0	19
Tuberculoid leprosy (males),	3	4	7	18	32
Tuberculoid leprosy (females)	7	4	3	4	18

The subjects tested are grouped in this table into "positive" and "negative" reactors, in terms of arbitrary scales, as defined.

matous leprosy, but late lepromin reactions tend to be smaller in the latter This difference may be due to inaccuracy in measuring the very small reactions In males with lepromatous leprosy there is a 90% probability that the mean twenty-eight day reaction size lies between 0 9 mm and 2 1 mm , whereas for controls at twenty-eight days the equivalent figures are 3 4 mm and 3 9 mm (table I) In adult males with tuberculoid leprosy the late lepromin reaction, as would be expected, is substantially greater than that seen in controls (mean twenty-eight day lepromin reaction 4 8–9 6 mm)

Skin reactions to both antigens in males with tuberculoid leprosy are usually larger than in females (table I) This is particularly true of the forty eight-hour tuberculin reaction This sex difference is not so clear cut in lepromatous leprosy, unless one omits the 12 males and 1 female showing no measurable reactions to tuberculin, and the 13 males and 7 females showing no reaction to lepromin at twenty eight days If a measurable reaction does result, the mean values are larger in males At twenty-eight days the trend is still present but less striking

There is some correlation between forty eight hour and twenty-eight-day lepromin reactions , but, except in the case of tuberculoid leprosy, it is smaller than might be expected (Fernandez 1940) The two reactions were not always parallel, and an appreciable late reaction was usually (but not always) preceded by a large early reaction In view of the type of antigen used, this feature is perhaps not surprising, and no emphasis can be placed on the late readings

It might prove useful to investigate late lepromin reactions on the basis of histological appearances in biopsy material from the site of inoculation This technique has been found to increase the diagnostic value of reactions to Nickerson-Kveim antigen in sarcoidosis (Siltzbach and Ehrlich 1954)

Discussion

In an investigation of this kind there are several difficulties in interpreting the results It has been claimed that tuberculin and lepromin sensitivities are positively correlated, and on the basis of this observation an immunological relationship between tuberculosis and leprosy has been postulated Such a thesis would be more easily tenable if the sensitivities involved indicated immunity in their respective diseases , but tuberculin sensitivity does not imply immunity to tuberculosis, and significant lepromin sensitivity is seen mainly, if not v, in the tuberculoid form of leprosy The be regarded as immunological factors only in so far as they reflect the capacity of the host's tissu to react to the corresponding antigens

In tuberculoid leprosy, skin sensitivity to lepromin is usually high , the disease itself is mild and self limiting suggesting a high resistance to leprosy bacilli From these observations it appears to have been inferred that high lepromin sensitivity is closely associated with high resistance , and, therefore, the production of lepromin sensitivity in uninfected people might protect them against infection For this purpose, B C G vaccination has been advocated Many workers have recorded increases in lepromin as well as tuberculin sensitivities after the administration of B C G vaccine to healthy subjects A large proportion of people with "negative" reactions to lepromin are stated to become "positive" after this measure (de Souza Campos 1953, Ferna 1943, 1951, Kocsard and Sagher 1953, Lowe and Mc 1953a) This observation is particularly intere Cochrane (1955) states that lepromin "conversion" i seen in patients with lepromatous leprosy who tuberculosis

The present investigation is not concerned with relationship of immunity and skin sensitivity, but with the possibility of there being some correlati between the sensitivities induced in man by infecti with tubercle and with leprosy bacilli In this pilot stud the degree of correlation established between tubercul and lepromin sensitivities was small, and was found on among the patients with pulmonary tuberculosis, th smallest of the three groups tested in the trial Further more the tuberculous patients showed a greater degr of sensitivity to lepromin than did the controls—thoug this may be merely a consequence of the former correlation In lepromatous leprosy, where lepromin sensitivity is slight or absent, a small proportion of the patie showed an intense degree of sensitivity to tubercul When these were excluded the two main groups of lepro patients did not show greater tuberculin sensitivity th the controls

In view of these findings there seems to be no sim and direct relationship between tuberculin and lepro sensitivities However, the observations in patients wi tuberculosis and lepromatous leprosy suggest the existe of a relationship of some kind

Summary

A pilot survey was made to investigate correlati between tuberculin and lepromin sensitivities in the South African Bantu

Three test groups were selected for the trial 10 patients with leprosy, 57 patients with pulmonar tuberculosis, and 114 healthy controls

In the controls and in the patients with leprosy no correlation could be established between lepromin and tuberculin sensitivities In the patients with pulmonary tuberculosis, however, a positive correlation was found Furthermore these tuberculous patients showed a greate degree of sensitivity to lepromin than did the contro

A small proportion of the patients with lepromatou leprosy showed a very high degree of sensitivity to tuberculin

I am greatly indebted to the medical superintendents and staff of the Westfort Institution, Pretoria, and the Waters Hospital, Johannesburg, for facilities and willing assistance to the British Tuberculosis Association for providing the lepromin, and to Dr R G Cochrane, through whose kin services it was made available , to Mr B Benjamin for his advice in planning the trial and for scrutinising the early results , to Mr P M Payne for his exhaustive statistic analyses of the complete findings , and to the Board of Governors of the Brompton Hospital for allowing a period of study leave during which this work was done Lastly, I should like to thank Dr R W Riddell and Dr J R Bignall, of the Brompton Hospital, for their advice, help, and encouragement

References at foot of next column

TRAUMATIC RUPTURE OF DIAPHRAGM WITH HERNIATION OF ABDOMINAL VISCERA

K. K. SINHA
F.R.C.S.
[illegible]

INDIRECT violence is one of the rarer causes of traumatic rupture of the diaphragm, and in most recorded cases the patient sustained gross injury to abdominal viscera. In the case described here the only abdominal organ to be injured was the spleen.

A woman, aged 45, was admitted to hospital a few hours after a car accident in which she had been thrown on to her right side and had felt a sudden snap all over the left side of her chest.

Fig. 1—Radiograph of chest showing high gastric shadow, collapsed left lung, and fractured ribs.

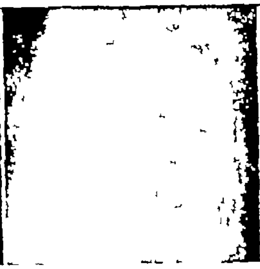

Fig. 2—Barium-swallow: œsophagus distorted and the stomach high in the thoracic cavity.

Fig. 3—Postoperative appearance: left lung re-expanded.

On admission her pulse-rate was 90 per min., blood-pressure 120/90 mm. Hg, respirations 20 per min. There was no cyanosis or evidence of respiratory distress, though she complained of pain in the left side of her chest. Bowel sounds were audible over the left hemithorax.

Radiography of the chest revealed fractures of the upper [illegible] ribs on the left side. The left lung seemed to be collapsed and the diaphragm appeared unusually high; the gastric shadow could be seen as high as the fifth left intercostal space (fig. 1). Barium-swallow showed considerable distortion of the œsophagus and confirmed the presence of stomach high up in the thoracic cavity (fig. 2).

Diagnosis.—The absence of respiratory distress was difficult to explain in view of the radiographically and clinically demonstrable collapse of the left lung. The problem was whether it was a case of congenital high diaphragm or a tear of the diaphragm with herniation of the bowel and collapse of the lung. The history of trauma along with the radiographic findings suggested a diagnosis of traumatic rupture of the diaphragm.

Progress.—The patient's general condition remained quite satisfactory. She had no difficulty in taking food, and the bowels continued to act normally for two days after admission. On the third day she started to vomit, and screening showed the [illegible] of [illegible] in the stomach. She was removed to the theatre [illegible].

Operation.—Thoracotomy was done through the bed of the eighth rib. Inside the left pleural cavity the spleen, stomach, transverse colon, [illegible] omentum, and small intestine were found. On the left side there was a large tear [illegible] from the front backwards, where the [illegible] the diaphragm [illegible] the muscular portion. The spleen was [illegible] but there was no [illegible] to suggest recent bleeding. [illegible] the chest [illegible] hæmorrhage began and splenectomy had to be done. The stomach was returned to the abdomen and the [illegible] of the diaphragm was [illegible]. The diaphragm was repaired with interrupted [illegible] stitches, and after the abdominal and thoracic [illegible] had been [illegible] the lung expanded [illegible] by the anæsthetist.

Postoperatively [illegible] recovery was uneventful, and bowel sounds returned within twenty-four hours. Oral feeds were begun within thirteen hours of operation. On the tenth day after operation the blood-pressure was 125/80 mm. Hg, and the apex beat had returned to the normal position. There was no abdominal distension. Breath sounds were clearly audible at the left base, though slightly diminished compared with the opposite side. Radiography showed satisfactory expansion and functioning of the left lung (fig. 3).

Noteworthy features in this case were that: (1) the patient's general condition remained good despite collapse of one lung and herniation of a large amount of bowel; (2) there was no evidence of shock at the time of admission; and (3) the ruptured spleen bled only when the chest was opened.

DIAPHRAGMATIC HERNIA FOLLOWING INJURY

P. A. HAMDI
M.B. Alexandria, Ph.D. Lond.
D. K. STURDY
M.B. Lond.
[illegible] DEPARTMENT OF [illegible], MORRISTON HOSPITAL, SWANSEA

IT is known that severe crushing injuries to the abdomen and chest may be responsible for rupture of the diaphragm with subsequent development of diaphragmatic hernia. Of 7 cases reported by Evans and Simpson (1950) 5 were due to severe crushing injury to the abdomen, 1 sustained bruising of the chest wall, and none had fractured ribs. Evans and Simpson suggested that the mechanism of the injury to the diaphragm was in the nature of an explosive rupture due to sudden increase in intra-abdominal pressure.

The case presented here illustrates how herniation of abdominal contents into the thoracic cavity revealed itself as an acute abdomino-thoracic emergency twenty-four hours after the injury.

Case report

A man, aged 40, was admitted semiconscious to the [illegible] surgical unit at 11.30 P.M. on May 8, [illegible], having been knocked down by a motor-car an hour previously. Immediately after the accident he had been given morphine gr. [illegible] by a [illegible] practitioner.

On admission he was easily roused but did not [illegible]. He had a laceration over the right eye [illegible] skull showed a comminuted fra

DR. KUPER: REFERENCES

[illegible] R. (1950) *Int. J. Leprosy*, 18, 441.
[illegible] R. G. (1951) Personal communication.
[illegible] Campos, N. (1953) *Int. J. Leprosy*, 21, 307.
Edwards, L. B., Palmer, C. E., Magnus, K. (1953) B.C.G. Vaccination. World Health Organisation Monograph Series no. 12. Geneva.
Fernandez, J. M. M. (1940) *Int. J. Leprosy*, 8, 1.
— (1943) *Ibid*, 11, 15.
— (1951) *Ibid*, 19, 474.
[illegible] J., [illegible] C. (1953) *Brit. med. J.* i, 36[illegible]
Hald, A. (1952a) Statistical Tables and Formulas. New York.
— (1952b) Statistical Theory and Engineering Applications. New York.
[illegible] (1953) *J. invest. Derm.* 21, 69.
Lowe, J., McNulty, F. (1953a) *Int. J. Leprosy*, 21, 173.
— — (1953b) *Brit. med. J.* ii, [illegible]
Meyer, S. N., Hougen, A., Edwards, P. (1951) *Publ. Hlth Rep. Wash.* 66, 561.
Palmer, C. E. (1953) *Amer. Rev. Tuberc.* 68, 678.
— Bates, L. E. (1952) *Bull. World Hlth Org.* [illegible]
[illegible] L. E., Ehrlich, J. C. (1951) *Amer. J.* [illegible]

Dr. Robert [illegible]
C. M. C. Medical College
53355

right superior and lateral orbital margins and a depressed fracture of the outer wall of the frontal sinus in the midline There were no abnormal neurological signs on examination nor any signs of shock, the pulse rate being 68, respirations 20 per minute, and the blood-pressure 150/80 mm Hg There were no obvious signs of injury to the abdomen or the chest The patient had passed clear urine since the injury

Operation —At 10 A M., next day, under general anæsthesia, the supraorbital wound was cleaned and excised, the fracture involving the orbital margins was reduced, and the wound was closed in layers

Postoperative Course —On his return to the ward the patient became very restless and began to vomit what appeared to be altered blood Later in the day he complained of pain in the epigastrium and breathlessness There was no shoulder pain The pulse rate had increased rapidly to 128 and respirations to 40 per minute, while the blood pressure had dropped to 90/60 mm Hg

On examination, the patient was extremely pale and sweating profusely, with anxious facies, and lying on his right side with his knees flexed The apex beat was 2½ inches from the midline in the fifth left intercostal space The heart sounds were normal The left side of the chest was immobile on respiration and dull on percussion as high as the third left intercostal space anteriorly There was complete absence of breath sounds over this area, and no adventitious sounds were heard There was good air entry in the right lung The abdomen moved normally on respiration, there was tenderness and guarding over the left hypochondrium and epigastrium, percussion revealed a normal area of liver dullness, and bowel sounds were absent Rectal examination revealed no abnormality A provisional diagnosis of ruptured diaphragm with hæmothorax was made, and in view of the rapidly deteriorating condition of the patient immediate operation was considered advisable

Second Operation —The abdomen was explored through a left paramedian incision. There was no free fluid or blood in the peritoneal cavity A large oblique tear, 5 inches long, was felt in the left cupola of the diaphragm The region of the left kidney and splenic flexure of the colon was contused The stomach and spleen had herniated into the left pleural cavity through the tear in the diaphragm A thoracotomy with resection of the left ninth rib was next performed, this rib was found to be fractured in the mid axillary line The stomach was much dilated and thin walled, with numerous subserous hæmorrhages As it could not be reduced through the diaphragmatic tear, its contents were aspirated, three pints of coffee coloured fluid being recovered The stomach and spleen were then returned to the abdominal cavity, and the tear in the diaphragm was sutured with 'Mersilene' The thoracotomy incision was closed with drainage of the left pleural cavity, and the laparotomy incision was closed without drainage Blood (2 pints) was given intravenously during the operation

Recovery was uneventful Daily radiography of the chest showed a completely expanded left lung, with a little effusion of fluid at the left base after the fourth day this effusion gradually resolved A month later a barium meal showed no evidence of intrathoracic herniation, and radiography of the chest revealed complete expansion of the lungs

Comments

This case is of interest because the abdominal contents must have herniated into the thorax after the administration of the first anæsthetic for suturing the supraorbital margin The stomach presented the picture of acute dilatation Most of the published cases of traumatic hernia have developed insidiously, appearing from a few days to many weeks after the original injury Frequently the diaphragmatic lesion had been overshadowed by more serious intrathoracic or intra abdominal complications

We have been unable to find any reference to the enormous gastric dilatation noted in the present case It seems likely that, at the moment of injury, the diaphragm ruptured explosively owing to increased intra-abdominal pressure Later on, during the induction of anæsthesia and possibly associated with straining, the tear became large enough to allow herniation of the stomach and spleen into the thorax, and the constriction at the hernial orifice caused great dilatation of the herniated stomach

This [illegible] illustrates the importance of making a [illegible] ical examination in cases of injury to the head, not only at the time of admission but also durin the ensuing stages of return to consciousness

We are indebted to Mr Norman Whalley for permission to publish this report

REFERENCE

Evans C J, Simpson, J A (1950) *Thorax*, 5 343

Preliminary Communication

HYALINE MEMBRANE IN THE LUNGS OF THE NEWBORN

IN recent years much work has been done to elucid the nature, source, and cause of hyaline membrane i the lungs of newborn infants Farber and Wilson[1] showed that similar membrane is sometimes formed i other conditions, and Farber[2] later demonstrated th œdema and membrane could be produced in rabbits b bilateral mid cervical vagotomy Others[3-6] have s shown that various experimental procedures may prod a similar disease pattern in the lungs of animals, and it generally agreed that a number of agents and proces may lead by one or more mechanisms to a comm histopathological finding

Histochemical analyses of the membranes[3-6] as foun in premature babies and in experimental animals hav established the presence of a polysaccharide aldehyd Wagner,[7] who has carried this a stage further, believ that the membrane contains mucoprotein and that it formed from endogenous mucus derived from the na pharynx, buccal cavity, and bronchial tree of the inf Other observers[3] have been unable to demonstrate mu in hyaline membranes by histochemical methods, this does not surprise us, since we have found that epithelium of the respiratory bronchioles is muc negative, and that the only mucus secreting gl present are sparse subepithelial acini Very rec Gilmer and Hand[8] concluded from morphological stu that the membranes are endogenous, and, by application of two methods hitherto not used in the st of this disease, we ourselves have come to the s conclusion Our methods seem to reveal both the nat and source of the membranes

Using frozen sections of formalin-fixed material, applied the Lepehne Pickworth benzidine nitroprus peroxide technique[9] By this method the erythroc were stained an intense blue black as expected, but hyaline membrane took on a uniform rich royal b colour The occasional blue black red cell could be eas identified as an entirely distinct body in the membra It was further noted that the epithelium of the respirator bronchioles and alveolar ducts showed a rich royal bl granularity, and in some cases this granularity was intense that the epithelial cells were seen as a unifor royal-blue The intensity of this royal blue staining the membranes and epithelium was somewhat less material which had been in formol saline for 3-5 month

At this stage we realised that we were dealing wit either organic iron or peroxidase enzyme, or both We then found that previous treatment with 5% sodium cyanide, or 5% sodium azide, or steaming for 5 minute in each case reduced the intensity of the royal blu staining, but did not abolish it However, we noted al that lengthy treatment of frozen sections by these method abolished the staining reactions by removal of the membranes and granules From these observations ar

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1 Farber S, Wilson, J L *Arch Path* 1932, 14, 437
2 Farber S *J exp Med* 1937 66 397
3 Blystad W, Landing B H Smith C A *Pediatrics*, 1951 8
4 Miller H C Behrle F C, Gibson D M *Ibid*, 1951 7 611
5 Tran Dinh De Anderson G W *Obstet Gynec Surv* 195 8 1
6 Bruns P D, Shields, L V *Amer J Obstet Gynec* 195 67 1224
7 Wagner J C *Lancet* 1954 ii 634
8 Gilmer W S, Hand A M. *Arch Path* 1955, 59, 207
9 Lillie R D. Histopathologic Technic Philadelphia 19 p 119

om the fact that the staining intensity was diminished ı material which had been fixed for a long time in rmol saline, we concluded that the reaction was due rtly to enzyme but mainly to organic iron

To test these conclusions we applied the NADI action to frozen sections by placing these in 1% alpha phthol (alcoholic) for 5 minutes and then for 5 minutes 1% aqueous dimethyl para phenylene diamine By is technique the hyaline membranes and granules in e respiratory bronchioles were stained a purplish blue the indophenol blue, the staining of the red blood-cells ing more intense but of the same colour Prior treat ent of the sections with cyanide, &c. was found to minish but not abolish the staining reaction

The lungs of several controls were examined by both chniques, and from these it was apparent that the tensity of the specifically staining granules in the spiratory bronchiolar epithelium was inversely pro rtional to the gestation age and that it was greater in ematures dying of hyaline membrane disease than in mparable prematures not having this condition owever, the intensity of the granularity was much less very premature infants (less than 1200 g) Further was apparent that the specific granularity of the ithelia of the respiratory bronchioles and alveolar cts increased with respiration since it was virtually sent in lungs atelectatic from birth and in those of llborn infants The œdema fluid in adult cases of rebral trauma and in cases of bulbar poliomyelitis was und to contain abundance of these specific granules enly scattered throughout the fluid and it was clearly ident that drying and condensation of such pulmonary dema fluid would lead to formation of a membrane hich would stain uniformly by the techniques used

It is very unlikely that these specific staining reactions the hyaline membranes are due to diffusion of material o the membrane In the first place the staining is o even for a diffusion phenomenon Secondly where uld this material come from except from the respiratory nchioles which we have shown to be laden with nules of the same staining reactions? Hæmolysis as use is also unlikely, because the reactions were found cases with no pulmonary hæmorrhage and because a case of hæmorrhagic pulmonary disease of the new rn, where hæmolysis was evident in the presence of t red cells the picture was patchy and uneven ally we have found that the two reactions work pletely and equally well in deep frozen unfixed lung ue from a case of hyaline membrane disease

It seems to us most likely that the common factor ponsible for the two reactions (Lepehne Pickworth d NADI) is the cellular respiratory enzyme system tochrome-oxidase/cytochrome C It is indeed possible at respiratory enzymes are produced in the granules hich we have demonstrated in the epithelia of the spiratory bronchioles and alveolar ducts and it is mpting to suppose that this enzyme system is an ive secretion of the epithelia An analogy may there o be drawn between infants developing hyaline embrane disease and the experimental rabbits of rber in that both probably suffer from an uncontrolled cretion of this enzyme system Further it is very obable that the actual hyaline membrane represents condensed and dried accumulation of this secretion, pecially as it is conceded that the only factor known modify the incidence and severity of this disease is gh humidity

We cannot at this stage be certain that the substance(s) ving rise to the reactions described here are cytochrome-idase/cytochrome-C since other metallic porphyrin otein complexes could be responsible for similar stochemical findings

MATTHEW J LYNCH
M.B M.R C.P

LES D MELLOR
F I.M.L.T S T

Department of Pathology
The General Hospital
Sudbury Ontario
Canada

Medical Societies

ROYAL SOCIETY OF MEDICINE

Metabolic Factors and the Infectious Process

THE section of pathology met on April 26 under the chairmanship of Prof L P GARROD the president to hear Prof RENÉ DUBOS, of the Rockefeller Institute, New York discuss the Effects of Metabolic Factors on the Infectious Process

Professor Dubos described experiments by which the expectation of life of mice infected with tubercle bacilli and also with strains of staphylococci salmonella, and klebsiella could be shortened. He had found that the expectation decreased when animals were exposed to various stresses" before inoculation A number of different stresses had been used including the administration of thyroxine or dinitrophenol, in such doses as to inhibit the animal's normal weight gain, or of sodium citrate and α keto glutarate The simplest method however, was starvation for thirty-six hours before inoculation and this method had given the most striking results. The results after starvation could not be explained simply by calorie deprivation for low-calorie diets adequately varied in constitution, which reproduced the effects of starvation, did not decrease the animal's resistance moreover the effects were observed too soon and were too quickly cured for this to be likely Nor was it simply weight loss that produced the effect for mice fed on diets so low in protein that their normal weight gain was offset were normally resistant to infection Professor Dubos had also shown that the most effective way of lowering resistance was by starvation for forty eight hours before inoculation and that recovery was complete after forty-eight hours on the standard Sherman diet On the other hand when the mice were fed with a mixture containing adequate fat, carbohydrate minerals, and vitamins but with essential amino acids in place of protein the state of increased-susceptibility was indefinitely prolonged Normal resistance was not restored until a whole protein was added. Not all proteins were equally effective in this respect and of those tested casein was the best

The results could be explained either by increased susceptibility of the animals to the bacterial toxins or by more rapid and extensive bacterial growth It had been found that, after thirty-six hours of fasting mice were more sensitive to endotoxins from gram negative organisms and to the recently isolated tuberculous toxin so that the LD$_{50}$ was reduced to a half or a third of that for normal animals Starvation for forty-eight hours, followed by a diet low in protein would reduce the LD$_{50}$ to a tenth But these comparatively small effects could not explain the observed change in susceptibility

In other experiments bacteria were injected intravenously in mice and later estimated quantitatively in various organs—with remarkable results Two groups had been studied: one had the standard Sherman diet (group 1) and the other had a diet low in protein and was then starved for forty eight hours (group 2) Both groups were inoculated with a dose of 10^{8} Friedländer's bacillus (group III) and their organs examined quantitatively for bacteria ten hours later with the following results

	Spleen	Liver	Blood
Group 1	0 0 18	1 1 0	Sterile
Group 2	12–6000	10–50 000	+ +

Similar results were obtained with other organisms—e.g staphylococci—and using other forms of stress, such as increased carbohydrate intake or thyroxine administration

Professor Dubos concluded that the effect of malnutrition was to impair the local bactericidal powers of tissues possibly through depression of the reticulo-endothelial system It has been shown (Berry and Mitchell) that if the Krebs cycle was poisoned the animal's resistance was likewise depressed Therefore it seemed that the observed change in susceptibility might be explained by (*a*) lack of cellular glycogen, or (*b*) decreased glycogenolytic activity by the cell, or (*c*) lowered levels of polycarboxylic acid in the tissues All these effects led to impaired clearing-power of the reticulo endothelial system, decreased bactericidal power of the tissues, and decreased resistance to bacterial toxins Impaired antibody formation could not be cited, for mice had no natural immunity to Friedländer's bacillus

Summing up, Professor Dubos made three points (1) susceptibility to infection in mice can change rapidly as a result of various stresses, (2) the effect is rapid in onset, and rapidly reversible, and (3) the factors concerned seem to be independent of those taking part in the host's normal physiological processes

Prof A A Miles discussed the vascular phenomena during the earliest stages of infection He had found that the local reaction to the subcutaneous inoculation of organisms could be abolished by adrenaline, and that if this was done survival of the inoculum was enhanced tenfold The effect could be obtained only if adrenaline was injected locally within four hours of the bacterial inoculum Similar results were observed when the complement was inhibited by 'Liquoid' When the experiments were repeated using the vole bacillus, adrenaline was found to have little effect, but liquoid greatly enhanced survival in the local lesions By using histamine or a globulin permeability factor the local lesion was reduced in size to that of one produced by a tenth of the inoculum in untreated animals

Dr D A Long spoke on hormone balance in allergy and immunity He emphasised the importance of choosing a laboratory animal which showed similar immune and allergic reactions to man and which responded similarly to hormones, if the results were to be extended to man He described a series of experiments by which he had shown that the guineapig was a suitable animal He went on to show that significant variation in allergic response was obtained with several hormones Anti- and pro-diabetic factors exerted an effect, and significant desensitisation of tissues had been obtained with a recently isolated and quick acting thyroid derivative Sensitivity to tuberculin could be related inversely to blood sugar levels, and partial pancreatectomy prevented the increased response seen after treatment with thyroxine, which therefore acted through the islets of Langerhans He concluded that immunity was probably due to the balance between insulin and cortisone at any one time

Dr G G Meynell discussed the protective function of the gastro intestinal tract against infection He had found that *Salmonella typhimurium* was killed at pH2 in two to three minutes He had also shown that if the gastro intestinal flora in mice were modified by the administration of streptomycin, their resistance to an oral dose of *S typhimurium* was decreased, and also that the organisms given by mouth could be recovered from the large gut This type of effect might be important in man

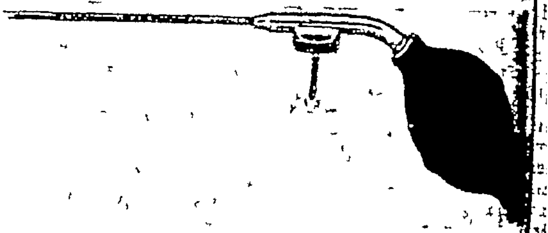
During the discussion, Dr Brian Lacey wondered whether sufficient attention had been paid to the genetic constitution, age, and sex of the mice used, and Dr A Felix, F R S, asked whether Professor Dubos's results were to be explained solely in terms of local cellular effects, or whether antibodies could account for some of them Professor Dubos felt that all the observed effects were probably mediated through a common channel, which facilitated both local tissue reactions and antibody

On the question of applying the results of ments to man, he said that no one knew better than he that mice and men were different, but justified the choice of a different animal when question to be answered by the experiment was sp and sufficiently limited

New Inventions

A MODIFIED THROAT SPRAY

In throat sprays used for spraying the throat bef endotracheal intubation or instrumentation, the b is joined to the nozzle by a flexible tube, with the r that the operator has to use both hands, and may the services of an assistant The throat spray illustr



here can be operated single-handed It is simple sturdy in construction, inexpensive, and effective T nozzle is long enough to be introduced between vocal cords for local preparation of the trachea. T Macintosh-type container keeps the volume of anæsthetic within safe limits and has the additi advantage of being unbreakable With a shorter noz the spray should also prove valuable in otolaryngology

The instrument can be obtained from Medical & Indust Equipment Ltd, for whose coöperation I am grateful.

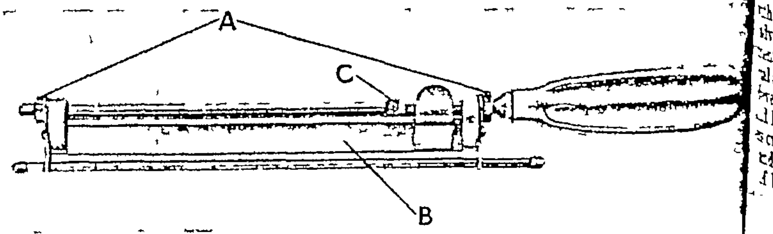
Mark Swerdlow

Manchester M.D, B SC Manc., F.F.A R C.S., D.A.

MODIFICATION OF HUMBY KNIFE

There have been several modifications of the orig Humby knife, with the aim of making it lighter *enabling the blade to be readily replaced and adj* In a new model, made at my suggestion by M Allen & Hanburys, these modifications have combined, and in this model the instrument need n dismantled to replace the blade Ease of sterilisation storage have also been considered

This new modified Humby knife is light and balanced Adjustment between the roller and the b from 0 01 mm to 1 0 mm is made by two kn collars (A) mounted on the back of the knife The bl



6¼ in long, is of the wafer-razor type and is lock securely in a leaf-spring holder (B) To fit a new bl it is only necessary to move a safety catch (C), open th leaf and insert the blade under the roller, and repla the safety catch

The knife without the blade can be sterilised b boiling, without risk of damage, and the blade sterili in the same manner as the standard interchangeab scalpel blades Since the blade can be fitted and remov quickly and easily, no protective cover is necessary f sterilisation or storage.

Fenton Braithwaite
O.B.E, M.A, M.B Camb.,
M.SC Manc., F.R.C.S
Plastic Surgeon

Royal Victoria Infirmary,
Newcastle upon Tyne

Reviews of Books

uroanatomical Basis for Clinical Neurology

TALMAGE L. PEELE, M.D., associate professor of anatomy in charge of neuroanatomy, Duke University School of Medicine New York and London McGraw Hill 1954 Pp 564 100s

MUCH has been said of the necessity for integrating ysiological and anatomical knowledge with subuent clinical training Most formal textbooks of atomy do, in fact, include paragraphs, usually in very ll print, devoted to applied anatomy Unhappily h excursions rarely succeed and it is often hard to cern the true links between form function, and ical disorder Dr Peele in this new textbook is very initely aware of the trefoil nature of this teaching blem and equipped with a practical training in earch neuro-anatomy and clinical neurology, he has ackled it in admirable fashion

After a short but adequate and well illustrated account the histological and embryological details of the nervous tem, he gives formal sections on descriptive anatomy of its ious components. In each section however there also pears comment on the physiological factors relating to the uctures described together with some of the more important hological changes to be expected and their clinical mani ations. Thus the account of the blood supply and ven ular system of the brain is followed by a short discussion he circulation of the cerebrospinal fluid a description of its mical and physical properties, and the clinical aspects of eased intracranial pressure Similarly the factual account he spinal cord is accompanied by physiological and clinical ail which though brief will at once inform and stimulate preclinical student In discussing recently acquired tomical knowledge Dr Peele maintains his standards nature and activity of the reticular formation are clearly cribed and recent electrophysiological work on the ebellum is succinctly presented. Some of this more con ersial evidence is perhaps offered a mite too firmly but teaching it is important to take up a reasonably definite itude. He is in any case to be congratulated on the healthy pticism he displays about the present evidence on the ppressor zones.

This admirable book is well illustrated and includes omprehensive bibliography

dern Trends in Ophthalmology

3rd series. Editor: ARNOLD SORSBY M.D., F.R.C.S London: Butterworth 1953 Pp 346 65s

Professor Sorsby is again to be congratulated on his rnational team of contributors, who give an admirable vey of knowledge which has not yet reached the tbooks. The book is arranged in sections dealing in n with the basic sciences on which ophthalmology s, advances in diagnostic procedures, clinical and erimental pathology clinical aspects in treatment, social aspects. Adequate space has been given to the st developments in anatomy physiology and patho- y and Professor Sorsby himself has contributed good pters on the nature of malformations, and on strepto- cin and the new antibiotics, as well as on the social pect of blindness. With Miss Mary Savory he also ites on cortisone and corticotrophin in diseases of e eye

ctions with Drug Therapy

HARRY L ALEXANDER M D emeritus professor of clinical medicine Washington University medical school Philadelphia and London W B Saunders. 1955 Pp 301 52s 6d

THE increased frequency of drug reactions in the past o decades has prompted Professor Alexander to compile s volume. He defines the reactions as lesions occurring only a small proportion of treated patients, differing om pharmacological effects and overdosage effects of e drugs and induced by therapeutic or subtherapeutic ounts

Only a few reaction patterns occur the main ones are matological manifestations, blood dyscrasias, serum sickness, shock, bronchial asthma, hepatitis, and polyarteritis nodosa. In the opening chapters of the book these patterns are described and their mechanism is discussed Controversial aspects of the subject are not fully discussed and this section is clearly not addressed to the specialist The general clinician may find the argument difficult to follow in places, and in many passages the syntax suggests overhasty revision. In the second part of the book many commonly used drugs and the reactions to which they give rise are described. Here the presentation is clear and informative and a coherent text replaces the catalogue common in works of this kind

Vitamins and Hormones

Advances in Research and Applications Vol XII Editors ROBERT S HARRIS professor of biochemistry of nutrition Massachusetts Institute of Technology Cambridge Mass; G F MARRIAN professor of medical chemistry University of Edinburgh; KENNETH V THIMANN professor of plant physiology Harvard University Cambridge Mass New York and London: Academic Press. 1954 Pp 303 $7.50

THE emphasis in this volume has been on vitamins, and consequently on nutrition; but three of the eight articles deal with hormones.

The first by John Hammond of Cambridge deals with the effects of light on hormone production and is concerned chiefly with seasonal changes, particularly those of reproduction which can be induced in warm blooded animals by modifying the illumination There is an interesting review by R B Bradbury and D E White (Western Australia) on œstrogens and related substances in plants, and one for practical men by F W Lorenz (California) on the effects of these œstrogenic hormones on the domestic fowl and their value in the poultry industry for fattening and other purposes. There are two papers on vitamin A—one by Saul H. Rubin and Elmer De Ritter from the Hoffmann La Roche laboratories, New Jersey dealing with the vitamin A requirements of animals, and the other by C Nieman and H J Klein Obbink of Amsterdam, dealing with the biochemistry and pathology of hypervitaminosis A . Both these papers are pertinent at the present time since the synthesis and large scale production of vitamin A has recently been effected by Hoffmann La Roche The authors give a valuable table summarising the dosages which have already proved toxic for man and the times for which they were administered Two English scientists, S K Kon and J W G Porter have contributed an account of that most complex but important subject the synthesis of vitamins in the ruminant: it now appears certain that the host and the micro-organisms in its rumen have established a nutritional symbiosis which is responsible for the provision of far more than the vitamins which the host requires. The article on the chemistry of vitamin B_{12} by Karl Folkers and Donald E. Wolf who are working in the Merck laboratories New Jersey is the most highly specialised and also the longest paper in the volume. The article by Charles S Davidson of Boston Massachusetts, on disturbances in nutrition relating to liver disease in man is a short and very readable account of current views on kwashiorkor alcoholic cirrhosis and other clinical disturbances in which the liver plays a prominent part

Doctors may be recommended to begin reading here; chemists, physiologists, and animal husbandmen will probably begin somewhere else in the volume but all may be recommended with confidence to begin.

A Handbook of Emergency Toxicology

A Guide for the Identification Diagnosis and Treatment of Poisoning SIDNEY KAYE B.S M SC associate professor of legal medicine Medical College of Virginia Springfield Ill Charles C Thomas Oxford: Blackwell Scientific Publications. 1954 Pp 303 42s

HE is a brave man who sets out to write an acceptable book on toxicology for the subject matter is about as inspiring as the contents of Bradshaw or a street directory Mr Kaye's great diligence shines out from the pages of his handbook but he has been no more successful than his predecessors in writing a best-seller

Upwards of 200 pages are occupied by a routine review of common poisons arranged alphabetically A telegraphic style is adopted this may be an advantage in a book designed for quick reference, but it inevitably makes this part of the text unreadable There is a table showing the names of the poisonous constituents of a large number of proprietary compounds —headache powders, weed killers, and the like Another table sets out the poisons contained in household articles—cosmetics, inks, matches, metal polish, and a score of the other perils that lie about us in our infancy It is difficult to imagine that anybody will get much help from the chapter on symptoms and signs to list 29 poisons and 15 diseases which may cause vomiting, purging, and abdominal pain does not suggest a very enlightened approach to toxicology, a few general principles would have been more valuable, especially if the subject could be correlated with physiology, pharmacology, and clinical medicine The author devotes only a paragraph to general considerations in this chapter, and the guidance here falls short A chapter on analysis provides a short survey of some of the chemical techniques of toxicology, but it is too meagre to interest the analytical chemist or the hospital biochemist In a book for students and practitioners, a competent essay on the collection of samples for expert analysis would be more valuable

Such books as this provide the best of all arguments for transferring the teaching of toxicology to departments of pharmacology, where the basic sciences are steadily ousting empiricism

Modern Trends in Psychosomatic Medicine

Editor DESMOND O'NEILL London Butterworth 1955 Pp 375 55s

PSYCHOSOMATIC medicine, though new in some of its aspects, is as old as medicine itself in others Some of the twenty articles in this fourteenth volume of the excellent *Modern Trends* series set out old and well-accepted views on the influence of the mind on the body, others offer less well-known and certainly less well-accepted ideas on a diversity of bodily, emotional, and psychiatric conditions The book contains most of the clinical evidence relating such disorders as thyrotoxicosis, ulcerative colitis, asthma, and skin diseases to psychological disturbances, and reviews the psychosomatic concept in medicine in general To the enthusiast it will offer a multitude of opinions confirming his belief that almost every illness is due to psychological stress In the sceptic it may provoke bewilderment and doubt that so much can be attributed with such confidence to such a cause, for though parts show a true and keenly scientific approach and parts are statistical, other chapters are mainly conjectural, and a few are almost frivolous The pleasantly classical and humanistic flavour of much of the writing is refreshing, and the references are copious and well chosen Dr O'Neill is to be congratulated on presenting such a full and varied picture of his subject, even if it may seem, perhaps inevitably, more one-sided than it should

Diagnostic Advances in Gastrointestinal Roentgenology

Selected Methods, with Clinical Evaluation ARTHUR J BENDICK, M D, director of radiology, Beth Israel Hospital, New York New York and London Grune & Stratton 1954 Pp 131 $6 00

IN the preface to this book the author states that "it is not intended for beginners but for radiologists of several years' experience, so situated that they cannot keep up with all the new techniques or the more modern interpretations of roentgen findings" Unfortunately it fails of this purpose, for it contains many inaccurate statements

Thus we are told that gravity does not play any appreciable part in the passage of barium from the œsophagus to the stomach, that the detection of neurological interference with swallowing is aided by demonstrating less distinct elevation of the hyoid bone on the films (but not how or under what circumstances), that the "club soda" technique in achalasia can be used as a method of deciding operability (but not how), and that amyl nitrate (not nitrite) is given to demonstrate the cardio œsophageal junction in achalasia We are told too "that the muscle of the diaphragm plays only a minor role in constricting the œsophagus at its lower end"

Th[illegible] not, on the whole, to be able to recommend a [illegible]ich a sound object

Antenatal and Postnatal Care (8th ed Lond J & A. Churchill 1955 Pp 672 37s 6d)—In p this edition of his reliable and senior textbook Prof F. Browne has had the collaboration of his son, Prof. J McClure Browne This family combination seems to worked well In including new work on the toxæmi pregnancy they draw attention to the work at the Wom Hospital, Sydney, Australia, where a determined campa to prevent eclampsia has resulted in a decline in inci from 1 in 400 in booked patients in 1946 and to 1 in 20,000 patients since, in the 1 failure, a ri blood-pressure had been overlooked The Brownes find t in every eclampsia patient there are one or more war signs which should lead at once to prophylactic treatment, their book does everything possible to ensure that th and other warning signs, in pregnancy and after, are missed

Alexander the Great and his Time (London Rock 1955 Pp 300 25s)—Dr Agnes Savill, well known as th editor of her husband's popular *System of Clinical Medi* has turned historian and here recounts the adventurous romantic story of Alexander the Great Alexander bec king of Macedon on the murder of his father, inheriting best equipped and trained army in the world At the age twenty he made himself master of Greece and began wonderful conquests marching from Macedon across t Hellespont to Egypt and from there through Persia to t upper reaches of the Indus in Hindu Kush When he d at the age of thirty three he had marched with his a nearly twenty two thousand miles often under unbeliev difficult conditions He fought innumerable battles, fre after a long forced march or a hurried climb up what enemy believed to be an unclimbable cliff or mount His weapons were surprise, swiftness of decision, imaginat foresight, ability to inspire and maintain the coöperati of his subordinates, and superb physical fitness and athl skill Dr Savill has written an interesting book. On left wondering whether she does not rebut too freely of the calumnies heaped on Alexander by some histor But if she tends to gild her lily, she leaves no doubt the reader's mind of the qualities that made Alexa great

Principles of Internal Medicine (2nd ed Lond H. K Lewis 1954 Pp 1790 £5 10s)—When the edition of this book by Dr T R Harrison and his coll was published in 1950, it was at once accepted as an auth tive textbook of American opinion The second e establishes it even more firmly as a standard work of ref The general arrangement is the same as before The third deals with general considerations and the rem considers the different systems of the body one by A new chapter on the general care of the patient giv useful review of nursing principles and the treatment symptoms in general The new edition is some 200 p longer than its predecessor, and with somewhat c print and some compression of space it contains a great more Chapter headings have gone and some of the illus tions have been much reduced in size The index has, great gain, been almost doubled in size The contribu now number 85, an advance of about 30 An important section of over 100 pages, which replaces the section weakness, is written by Dr R D Adams and his associ and includes an excellent and lucid account of the an states, depression, sleep disorders, fits, delirium, co and the psychoses

I was a Drug Addict (London Rider 1954 Pp. 15s)—Although Mr Leroy Street assures us that his acc is "uncoloured" the literary form evidently owes much to collaborator, Mr David Loth, who is a professional wri Fewer sentences such as "these homely objects were abo convey a new meaning to my specially alerted brain," fewer verbatim conversations would make the aut graphical statement seem more authentic As it sta however, it describes, in rather exaggerated language subjective experiences and the companionship which drug addict meets in his descent There is no obv improbability in all this, except for the happy ending w represents permanent recovery as the outcome of a fortu self directed plan for reducing the dose of morphine grad The work has social rather than medical or psychol interest

THE LANCET

LONDON SATURDAY MAY 14 1955

Orbital Leucotomy

STANDARD leucotomy, or lobotomy developed y **FREEMAN** and **WATTS** in which a large part of the refrontal areas is severed from the rest of the brain, as of late been carried out only in cases of long anding mental illness with severe behaviour dis der Apart from the unpredictability of its atomical results it commonly causes undesirable rsonality changes These changes, it was observed, re more likely to occur when the operation had en extensive and attempts were therefore made to ut it to a minimum Clinical observation of tients with frontal lobe injuries, as well as experi ental work, suggested that a regional factor was portant Several workers reported satisfactory sults from "lower quadrant" operations aimed at lating only the orbital part of the frontal lobes hese, like the standard leucotomy, were still blind ocedures lacking in precision With the increasing e of open operations various selective methods have en developed. One of the most interesting of these the undercutting of certain parts of the frontal rtex first proposed by **SCOVILLE**[1] who compared e effects of undercutting three cortical areas with ose of standard leucotomy The areas chosen were e superior surface of the frontal pole the orbital urface, and the medial surface of the cingulate gyrus e found that in schizophrenia and the affective ates undercutting the superior or the orbital surface ought about the same results as the standard eration, but with less personality defect. He garded undercutting of the orbital surface 'as e ideal operation for psychoneuroses and the milder ood disturbances because of the almost complete bsence of personality changes There was much o recommend the choice of that particular area for atients with otherwise intractable anxiety and epression

The importance of this area as part of the cerebral ubstrate of emotional integration is now generally ecognised **TOW** and **LEWIN**[2] described the results f undercutting the orbital surface in twenty patients ith various mental disorders who were subsequently followed up for two years. The effects were comparable with those of the standard operation, but the personality changes were less pronounced. Two reports on earlier pages of this issue appear to confirm the value of the method Dr **STRÖM OLSEN** and Mr **NORTHFIELD** have applied it to a group of patients with chronic neurotic tension states, in each of these patients, including one with pronounced paranoid ideas, depression was prominent More than half recovered from their symptoms and personality changes were slight Another group, suffering from long standing schizophrenia with personality deterioration, did less well Mr **KNIGHT** and Dr **TREDGOLD** report on a series of fifty two patients subjected to a slight modification of cortical under cutting Their results are almost as impressive as those of **STRÖM OLSEN** and **NORTHFIELD** They also found that improvement was most striking in patients with anxiety and depression Patients with hysterical symptoms did not respond favourably The two reports confirm the beneficial effect of orbital under cutting and the absence of severe postoperative personality changes, but it is difficult to compare the results in detail since these were differently assessed. **KNIGHT** and **TREDGOLD** eschew the term recovered" used by the other group of workers, but it can be assumed that the majority, if not all, of their "much improved" patients would have been classed among the "recovered" by **STRÖM OLSEN** and **NORTHFIELD** Evaluation and classification of therapeutic results is a serious problem in psychiatry, and communication between workers in the same field is often bedevilled by the pitfalls of semantics

The fact that an operation as limited as orbital undercutting can produce a substantial and often dramatic change in the mental state seems at first to contradict the view held by earlier workers that the degree of improvement depends chiefly on the amount of brain substance isolated **MEYER** and **BECK**[3] suggest that, though the extent of the operation is important regional localisation of the cut within the frontal lobe also influences the effects They point out that some very limited regional cuts may in fact, by severing the thalamofrontal projection, isolate large areas of cortex The question, therefore whether the frontal lobe functions by mosaic or mass action has still not been finally answered In their experience, the extent of the cut, wherever localised is correlated with improvement But various types of improvement follow surgical interference with frontal lobe function one is the complete disappearance of symptoms, especially of depression, immediately after the operation almost any operation on the frontal lobe however limited has sometimes resulted in this dramatic change In such instances at any rate, improvement or even recovery does not seem to have been bought at the price of a severe personality change, so obvious in other patients The results of cortical undercutting show that notoriously reversible symptoms, such as depression and anxiety, can be removed sometimes by a very limited operation—an effect which, though profound, is clearly unrelated to the personality change

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[1] Scoville, W. B. *J. Neurosurg* 1949, 6, 65 *Proc. R. Soc. Med* 1949, 42, suppl 1, 3

[2] Tow, P. M., Lewin, W. *Lancet* 1953, ii, 644

[3] Meyer, A., Beck, E. Prefrontal Leucotomy and Related Operations Edinburgh, 1954

In what type of patient can one expect such a distinct improvement ? Here we are still in the dark STRÖM-OLSEN and NORTHFIELD consider that neuropathology may some day provide the answer Some workers believe that it will eventually be possible to produce lesions to suit every condition and every patient The fact that the results of a precise and limited operation, such as orbital undercutting, are still inconstant, suggests that the effect does not depend only on the extent and localisation of the lesion The patients' personality—the sum total of his response patterns, innate and acquired—must be of considerable importance Only when we know more about the reactions of the personality to sudden alterations in the emotional charges shall we be able to predict the effects of surgical treatment in individual cases The psychiatrists, it is true, have been aware of this, and have generally accepted that in well-integrated personalities the likelihood of undesirable postoperative behaviour features, even after extensive operations, is small, but beyond this we know very little Naturally, clinicians are more interested in their successes, especially when a method has still to be established But the time comes when careful and systematic study of failures and partial failures is at least as important as that of successes This is particularly true in the present stage of the surgical treatment of mental disorders Such studies would also act as a wholesome corrective to the danger of a reversal to "atomistic" concepts of cerebral function The effects of localised operations on mental states have contributed to a revival of concepts reminiscent of those so persistently criticised by HUGHLINGS JACKSON, and a language has crept back into medical writings which not so long ago seemed almost extinct What would JACKSON have thought of the "intellectual pathways" referred to by KNIGHT and TREDGOLD ? The passage from LE GROS CLARK cited by these workers, and MEYER and BECK's[3] recent warning against too atomistic an interpretation of the effects of brain operations, show that at least some of those most familiar with cerebral structure and functions are opposed to a return to the old-fashioned rigid localisation of functions Only by taking into consideration the undamaged parts of the brain and the reactions of the whole personality shall we reach a fuller understanding of the scope and limitations of the surgical treatment of mental disorders

Estimation of Blood-loss

THE most important cause of shock after surgical or accidental injury is loss of blood into and from the damaged tissues, or of plasma in cases of burns and scalds, or of crushing Such shock usually responds to the rapid replacement of the lost fluid, but measurement of the amount lost, even at operation, is not easy

Estimates based on impressions during the operation are usually too low, even when reinforced by collection of the swabs, towels, and gowns Surgeons who have not submitted themselves to the discipline of direct measurement of blood-loss usually find it hard to believe the figures obtained in this way Som for example, when the operation is for arance of viscera in the pelvis or of a large block of organs in the upper abdomen—estimates based on impressions are of hardly any value, and when, in addition, the operation lasts many hours and is accompanied by transfusion to replace lost blood, direct measurement is especially necessary To be useful the method of direct measurement must provide an accurate answer shortly after the operation has ended Probably the simplest way is to wash out all the swabs, towels, gowns, and instruments in a known volume of water, to which is added the contents of the suction bottle The hæmoglobin level of this fluid is then measured either directly[1] or after conversion to acid hæmatin[2,3] This, together with the hæmoglobin level of the patient's blood before and immediately after operation, gives a fairly accurate guide to the volume of blood lost. PAQUIN et al[4] have devised a method suitable for cases in which blood or other intravenous fluids are being administered The difference between preoperative and postoperative weight is corrected on the one hand for additions (including dressings and transfused blood or other fluids), and on the other hand for depletion by bleedings, estimated insensible water-loss, resected tissue, and excreted urine and other lost body-fluids As a check they also measure blood-loss directly,[5] by weighing the towels, swabs gowns, and suction-fluid They have found close agreement between the results by these two methods, even for operations lasting ten hours with a blood-loss of over 4 litres But they point out that serious errors may arise from the accumulation of shed blood in "dead spaces"—for example, the pelvis—and from excretion of urine or, in operations on the urinary tract, from contamination of blood with urine Furthermore the method of PAQUIN et al cannot be expected to give really reliable results until we know more about the possibly wide variation in insensible water-loss during different types of anæsthesia and they themselves emphasise that their method should be combined with clinical examination before deciding on treatment Fortunately operations lasting for more than three hours are rare, and the amount of blood lost at operation seldom exceeds 2 litres

Measurement of blood or plasma lost by accidental injury is even less easy Theoretically such loss would be best measured by estimating the amount of blood remaining in the circulation and subtracting this from the normal volume, which, as GIBSON and EVANS[6] showed, is closely related to body weight But this approach is so studded with pitfalls that others have been tried NOBLF and GREGERSEN[7] found that in civilian injuries blood loss depended largely on the extent of muscle damage and the number of fractures, and GRANT and REEVE[8] showed that in limb injuries the volume of damaged tissue was a good guide to the volume of blood lost Mr RUSCOE CLARKE and his colleagues[9] have measured the increase in the volume of injured limbs nd also the red blood cell volume, and have stablished that estimates of blood loss based on hese two measurements agree closely. Their findings confirm the close relation of blood loss to muscle njury, which is particularly severe in fractures nvolving the shaft of the femur or the pelvis. Nevertheless, although the bleeding associated with such njuries is commonly underestimated, there is still nsufficient evidence to justify the very large transfusions of blood recommended by PRENTICE et al.[10] Early surgical treatment should be combined with rapid transfusion of enough blood to maintain the blood pressure within normal limits. The anæmia which follows severe injury presumably reflects the general post-traumatic protein katabolism, and should not be treated prophylactically by the administration of blood in excess of that needed to restore circulatory efficiency.

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[1] Oppenheim A Pack G T Abels J C Rhoads C P Ann Surg 1944 119 865

[2] Gatch W D Little W D J Amer med Ass 1924 83, 1075.

[3] White M L Buxton R W J thorac Surg 1942 12 10

[4] Paquin A J, Marshall, V F Nathanson B Ann Surg 1955, 141 53

[5] Wangensteen O W Minnesota Med 1942 25, 783

[6] Gibson J G jun, Evans W A jun J clin Invest 19 16 317

[7] Noble R P Gregersen M I Ibid 1946, 25 158 172

[8] Grant R T, Reeve, E B Spec Rep Ser med Res Coun Lond 1951 no 277

[9] Clarke R, Topley E, Flear C G T Lancet, March 26 19 p 629

The Mystery of Dental Caries

DECAYED teeth have caused the human race suffering and unhappiness for several thousand years. In ancient times dental caries was associated with the idea of worms in or around the teeth, and this notion persists in the primitive cultures of today. It seems that a certain JAQUES HOUILLIER (1498–1562) first cast doubt on the existence of dental worms, but that did not prevent GOTTFRIED SCHULZ, who lived at about the same period, from declaring that the application of gastric juice from a pig would expel worms—some even as large as an earthworm—from a decayed tooth.[11] GALEN believed that dental caries was produced by an abnormal condition of the blood which affected the internal structure of the tooth, and recent work gives some support to this hypothesis. The suggestion that micro-organisms might be responsible for caries was first put forward by LEBER and ROTTENSTEIN in 1867.[12] A few years later, MILLER,[13] working in KOCH's laboratory in Berlin, found that micro-organisms obtained from carious dentine produced lactic acid when cultured in the presence of sugar or starch, and he formulated the "chemico-parasitic" theory of dental caries. In 1925 BUNTING and PALMERLEE identified the commonest acid-producing organism in the mouth as *Lactobacillus acidophilus*.

The chemicoparasitic theory, together with the belief that dental caries is associated with the consumption of small molecule carbohydrates that are readily fermented, has been widely accepted for some fifty years. There is now much evidence supporting the theory, including the increased incidence of caries among Eskimos when refined carbohydrate foods were added to their normal diet.[14] Investigations during and after the wars of 1914–18 and 1939–45 also seemed to suggest that when sugar was rationed and other highly refined carbohydrates were scarce the incidence of dental decay in children dropped sharply, whereas it rose again sharply in the post-war years. More recently many research workers have come to believe that the incidence of caries is influenced by other factors—the structure of the tooth, conditions affecting the metabolism of the body, and the ingestion of fluorides in drinking water. Some workers now believe that caries is initiated by proteolysis of the organic constituents of the enamel and that decalcification is secondary.

A report just issued by the Medical Research Council[15] throws considerable doubt on the idea that caries in children is caused, at least partly, by excess of sugar in the diet. This report describes trials in London, Liverpool, and Sheffield on the effects of adding extra sugar to the diet of children in residential homes. The incidence and spread of dental decay in groups of children aged 2–14 years, was first observed for a year, during which the children received their normal diet containing liberal amounts of milk, fresh fruit, and vegetables, and, in most cases, supplements of cod-liver oil and orange juice. The children were then divided into two groups: one continued to receive the normal diet, while the other received additional white sugar. The dental condition of this group was compared with that of the controls at the end of 1, $1^{1}/_{2}$, and 2 years. Since work by OSBORN et al.[16] had suggested that unrefined sugar might contain some factor which tended to protect the teeth from attack by caries, raw sugar was included in the diets of some of the test children. The diets were arranged so that the control groups received 11 oz. of sugar a week, while the test groups received just over 22 oz. of white sugar or about $21^{1}/_{2}$ oz. of raw sugar. The results were somewhat unexpected. Despite the relatively large differences between the amounts of sugar given to the control and to the test groups there was no significant difference in the incidence or the spread of dental caries during the 2 years. There were some anomalous findings—for instance, some of the children who received extra white sugar actually had a significantly smaller incidence of caries than the controls—but these findings showed no consistency when the results were surveyed as a whole. There was no evidence that sugar affects the two dentitions differently. As far as could be ascertained, unrefined sugar does not contain a caries-inhibiting factor.

None of the children in the trial groups received more than about 4 oz. of sweets a week, and the report does not prove or even suggest that unlimited sweets are harmless. Mr. E. B. DOWSETT, in his presidential address to the British Dental Association in 1951, suggested that sweet-eating by children should be controlled.[17] In his view sweets made from glucose—as many now are—are more dangerous to the teeth than those made from sucrose. The problem of caries is undoubtedly in the broadest sense dietetic. But what aspect of the diet is at fault? Is there a local and external effect on the tooth, or is it systemic and internal? These possibilities are not mutually exclusive, and if the latest report has done no more than eliminate another hypothesis, that at least brings us one stage nearer the solution.

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[10] Prentice, T. C., Olney, J. M., jun., Artz, C. P., Howard, J. M. *Surg. Gynec. Obstet.* 1954, 99, 542.

[11] Guerini, V. A History of Dentistry. Philadelphia, 1909.

[12] Leber, T., Rottenstein, J. B. Dental Caries and its Cause. Translated by Chandler, T. Philadelphia, 1883.

[13] Miller, W. D. Micro-organisms of the Human Mouth. Philadelphia, 1890.

[14] Price, W. A. Nutrition and Physical Degeneration. California, 1945. Waugh, L. M., Donald, B. *Amer. J. Dis. Child.* 1911, 39, 193.

[15] King, J. D., Mellanby, M., Stones, H. H., Green, H. N. The Effect of Sugar Supplements on Dental Caries in Children. *Spec. Rep. Ser. med. Res. Coun., Lond.* no. 288. H.M. Stationery Office, 1955. Pp. 55. 4s.

[16] Osborn, T. W. B., Noriskin, J. N., Staz, J. *J. dent. Res.* 1937, 16, 165.

[17] See *Lancet*, 1951, ii, 71.

Annotations

REGULATION OF CARDIAC PERFORMANCE

Starling's classical work on the isolated dog heart demonstrated that the strength of its contraction, and therefore stroke output, was determined by diastolic ventricular volume This accorded with expectation, since the strength of contraction of striated muscle is, within physiological limits, determined by the initial length of its fibres In recent years Starling's law has been much discussed in relation to adaptation of the heart to disease, and an exceptionally well documented symposium on this important topic has now been published [1–9]

Three different sets of observations must be considered (1) on the isolated heart preparation where reflex, nervous, and hormonal influences are excluded, (2) on healthy intact mammals, and (3) on patients with heart disease

In the isolated heart the validity of the Starling principle is accepted,[5] but its exact mechanism is still disputed [6] "Venous return" is often said to determine cardiac output, but in any balanced state of the circulation venous return must be the same as the cardiac output Increased diastolic filling of the heart is much more likely to result from increased venous pressure, and this can occur physiologically by contraction of the spongework of venules and other small peripheral vessels pushing more blood towards the centre Guyton [3] has elaborated the conception of "mean circulatory filling pressure," which is the external squeeze of vessels on their blood content with flow factors eliminated This can be measured experimentally during induced temporary ventricular fibrillation, after which rhythmic cardiac contractions are re started by electric shocks As might be imagined, this "static" filling pressure rises with increasing volumes of blood in the circulation Though most of Starling's data showed a correlation between venous filling pressure and cardiac output, Starling himself appreciated that the filling of the heart might sometimes be greatly increased by very small pressure changes Katz,[10] using Wiggers's methods of accurate optical recording, showed that changes in cardiac output paralleled end-diastolic ventricular pressure It is, of course, better to estimate cardiac performance as *work* rather than simply as *output* Sarnoff,[2] who has re-studied the whole matter, has shown a linear correlation between venous filling pressure and *right* ventricular work, and when the left ventricle was loaded by increasing aortic resistance, pressure rose in parallel in the *left* atrium but not in the right Homolateral correlation is thus of the greatest importance For any given filling pressure the work of individual hearts could be increased by adrenaline or decreased by experimental restriction of coronary flow [2]

In intact animals and man the situation is more complex, since the heart is innervated and is exposed to varying amounts of endogenous adrenaline and other influences which may counteract the influence of changes in venous filling pressure End-diastolic volume and pressure may not always correspond if muscle tone can alter [1] While McMichael and Sharpey-Schafer [11] showed a significant general correlation between cardiac output and venous filling pressure in man, Warren et al [12] emphasised the exceptions to this rule Gregg et al[4] have found in the whole dog a general correlation between cardiac output and filling pressure when raised by intravenous infusion, but the correlation was not clear at lower rates of *infusion* Gauer [7] demonstrated close correlation between diminishing heart volume and stroke output in monkeys subjected to centrifugation Hamilton [9] reminds us that in many experiments with isolated animal hearts the outputs are artificially set much lower than the expected normal for the particular animal; Starling's law *might* be particularly easy to demonstrate under these conditions Richards [8] calls attention to the Swedish radiographic studies of heart volume, which show clearly that in exercise the heart increases in size only very slightly The increased output of effort is certainly brought about by increased rate and increased emptying of the ventricles—increased emptying has been of special interest since it was realised that under resting conditions the ventricles almost certainly do not empty completely and contain some residual blood at the end of systole

In patients with heart failure due to intrinsic heart disease the output tends to be relatively fixed, dropping to subnormal levels in the more advanced stages Heart rate in failure also tends to settle round 100 a minute Such hearts seem, like the kidney in advanced nephritis, to have lost their flexibility of response With this loss of fine adjustment, Starling's law may be the last resource of adaptation to pathological conditions In failing hearts the common absence of increase in cardiac output during exercise, despite a rising venous filling pressure, and other observations led McMichael and Sharpey Schafer [13] to the hypothesis that the failing heart behaves as though it were no longer responding normally to increases in venous pressure, such increases could even be accompanied by a falling cardiac output, and, conversely, lowering of venous pressure by venesection could be followed by improvement in cardiac output These observations may have to be considered in a new light, for Sarnoff [2] has pointed out that *decreasing stroke work at high filling pressure* is attributable to regurgitation through the atrioventricular valves The studies of Korner and Shillingford [14] show that some tricuspid incompetence is often present in heart failure The extent of this incompetence and its part in producing the congestive features of heart failure have not yet been fully appreciated

POLIOMYELITIS REVIEWED

WITHOUT doubt the great advances in our knowledge of poliomyelitis in the last few years began with the discovery by Enders, Weller, and Robbins [15] in 1949 that poliomyelitis viruses *could readily* be grown in tissue-cultures—a discovery which won them the Nobel prize in physiology and medicine for 1954 Thereafter our knowledge of epidemiology, pathogenesis, and prevention expanded at a great rate, and the new ground explored has lately been reviewed in a World Health Organisation *monograph* [16] In this Enders himself gives a beautifully clear exposition of tissue-culture techniques as applied to poliomyelitis, and Rhodes, Wood, and Duncan illustrate the application of these techniques in laboratory diagnosis Gard writes about the virus itself—*Poliovirus hominis* and the related *P muris* to use the correct terminology The new tissue-culture techniques have been applied first to urgent practical problems, and most of our theoretical knowledge of the virus is still based on earlier studies of infected nervous tissue, in which the virus may represent only a

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1 Katz L N *Physiol Rev* 1955 35 91
2 Sarnoff S J *Ibid* p 107
3 Guyton A C *Ibid* p 123
4 Gregg D E, Sabiston D C, Theilen E O *Ibid* p 130
5 Lorber, V *Ibid*, p 137
6 Rushmer, R F *Ibid* p 138
7 Gauer, O H *Ibid* p 143
8 Richards D W *Ibid* p 156
9 Hamilton W F *Ibid*, p 161
10 Katz L N *Amer J Physiol* 1928, 87, 348
11 McMichael, J Sharpey-Schafer E P *Brit Heart J* 1944, 6, 33
12 Warren J V, Brannon E S, Stead E A., Merrill, A J *J clin Invest* 1945 24 337
13 McMichael J Sharpey Schafer, E P *Quart J Med* 1944 37 123
14 Korner, P Shillingford, J *Brit Heart J* 1954, 16 447
15 Enders, J F Weller T H, Robbins, F C *Science* 1949 109 85
16 Poliomyelitis World Health Organisation Monograph Ser no 26 Geneva, 1955 pp 400 40s Obtainable from H M Stationery Office, P O Box 569 London S E 1

millionth to ten millionths of 1% of the tissue It is therefore important to re-examine the properties of the virus grown in the more satisfactory milieu of tissue culture now available; to take only one point it is vital for vaccine production to know the resistance of the virus to different forms of inactivation Methods of inactivating virus on the skin are scarcely of less interest, since there is still a possibility that virus on the skin may be implanted by injections and on this matter Gard says "It can only be stated that, as a means of removing or inactivating virus on the skin the use of soap detergents, ether ether alcohol, or chloramine is nothing but a symbolic ritual only iodine might be expected to serve the purpose

Hammon describes the first stage in the striking progress in protection—passive immunisation with gamma-globulin The first large-scale trials in 1951 and 1952 showed that gamma globulin gave some temporary protection against paralytic poliomyelitis, and later work has demonstrated that the all important subclinical infections were not prevented. But mass administration of gamma globulin during epidemics has been disappointing and its use for prophylaxis of contacts cannot now be recommended for the first detected case in a family is seldom the first to be infected Hammon suggests that gamma globulin may be most useful in dealing with outbreaks of poliomyelitis in summer camps and boarding-schools. It is clear however that active immunisation is the main hope in preventing poliomyelitis, and in the monograph this subject falls to Sabin and Koprowski Sabin discusses immunity as a result of natural infection of man or experimental infection of animals with special reference to vaccination, and he is much concerned with variations in virus virulence Tissue-culture methods allow the detection of naturally occurring viruses of low virulence, and Sabin s important laboratory experiments have segregated avirulent virus variants which might later be used to immunise man. As we pointed out in a leading article last month[17] both Sabin and Koprowski believe that live avirulent poliomyelitis virus will prove best in the end; and this view may well find wider support when the difficulties that are now besetting the immunisation programme in the United States have been fully investigated Sabin and Koprowski have made considerable advances both in preparing avirulent variants from all three antigenic varieties of virus and in testing some of them in man There are many difficulties ahead in this field, but there is no reason to believe that they cannot be overcome in the next few years On p 1018 we report some of Sabin s latest findings which he described to a meeting of the Association of American Physicians last week

Our outlook on the epidemiology of poliomyelitis has also undergone some sharp changes of late, and these are discussed in the monograph by Paul Gear and Freyche and Nelson Poliomyelitis is world wide and in nearly all countries paralytic cases have become commoner and the disease has attacked older people The virus has spread widely however in underdeveloped countries where the disease has the characteristics of ' infantile paralysis —that is paralytic cases are less common in adults and are largely confined to infants widespread subclinical infections in infancy protecting against paralytic disease in adult life Similarly the first recorded epidemics in Scandinavia North America Australia and New Zealand fifty to seventy years ago were all infantile paralysis. The sparing of adults suggests that they were protected by previous subclinical infection, and it need not be assumed that this was a new disease The changed characteristics of poliomyelitis have in fact been created by our changed hygienic habits Poliomyelitis is today under pressure to spread from underdeveloped areas into a susceptible population and if the inter-epidemic period is long the risk of a severe epidemic increases annually One of the most graphic examples of this is the Hudson Bay epidemic in 1948–49 when 60% of the Eskimoes had paralytic disease, all age-groups were involved the lowest clinical attack rate being in the infants Gear mentions another fact which brings home the changing pattern of poliomyelitis in Nyasaland and Southern Rhodesia paralytic poliomyelitis is today one of the most serious hazards facing newly arrived adult European settlers. Discussing public health measures, Payne points to the anomaly that so far as poliomyelitis is concerned hygienic measures may have done more harm than good He suggests that early in an outbreak, or with inter-epidemic cases, the application of hygienic measures may prevent an epidemic from starting once it has started the large number of sublinical infections makes further steps of this kind valueless

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[17] Lancet April 23 1955 p. 851

PANCREATITIS

MODERN treatment has greatly changed the clinical course of acute pancreatitis as Kirby et al.[1] have shown by comparing cases admitted to the Hospital of the University of Pennsylvania before 1946 with those admitted in subsequent years Of 80 patients in the twenty five years up to 1946 23 (29%) died the majority from vascular collapse shortly after the illness began in 1946–53 110 patients were treated with 21 deaths (19%) Deaths in this second group took place later only 3 (14%) of the 21 deaths took place in the first week of the illness compared with 20 (90%) of the 23 in the earlier group The manner of death has also apparently changed Secondary hæmorrhage which was not observed before 1946 accounted for 11 deaths in the second group and in this group of those patients with hæmorrhagic pancreatitis who survived about a quarter bled either from an abdominal wound or into the alimentary tract Possibly antibiotic therapy has reduced the early toxic effects due to infection, so patients survive long enough for the erosive pancreatic enzymes to damage vessel walls and thus precipitate secondary hæmorrhage; Kirby et al. suggest that this complication may be prevented by proper drainage to encourage the escape of the enzymes.

The most severe form of acute pancreatitis was found after operations involving the pancreas There were 14 such cases with 8 deaths 7 from hæmorrhage In 6 of these 14 cases the pancreatitis followed subtotal gastrectomy in 5 subtotal pancreatectomy in 2 simple biopsy associated with cholecystectomy and in 1 colectomy for a growth adherent to the pancreas Obstruction of the pancreatic ducts is known to be a potent factor in precipitating pancreatitis[2] which for this reason is sometimes found in conjunction with carcinoma It is therefore not difficult to understand why pancreatitis follows operations such as gastrectomy or *pancreatectomy*, that may cause trauma to the pancreatic ducts But this does not explain all cases Millbourn[3] has drawn attention to the possibility of interference with the blood supply to the pancreas by damage to the superior and inferior pancreatico duodenal arteries but Warren[4] points out that the blood-supply is so generous that ligation of one artery alone would be unlikely to cause trouble Pancreatitis has arisen as a late complication of partial gastrectomy, through stagnation in the afferent loop and suggested causes include spasm of the sphincter of Oddi and sludging of pancreatic secretions within the ducts as a result of medication and dehydration[5]

Injury *to the ducts* is the most important cause of postoperative pancreatitis not only because it is probably the commonest but also because it should be treatable—if not avoidable In Warren's [4] 7 cases of pancreatitis following partial or total gastric resection, 6 of the patients died with pancreatic necrosis In 4 of these a penetrating duodenal ulcer was reported, in any of these 4 cases a duct may have been damaged, while in a 5th carcinoma of the stomach may have involved the pancreas The pancreatic duct, the accessory pancreatic duct, or both, were damaged at operation for duodenal ulcer on 6 other patients, 3 were spared *pancreatic obstruction by the development of a fistula*, which healed subsequently or was successfully implanted into the intestine, and in 3 the ducts were reimplanted at the outset, all survived and pancreatitis did not ensue It is not easy to observe either of these ducts lying in inflammatory tissue near the base of a duodenal ulcer, owing to their smallness it is still less easy to reimplant them when they are seen, unless they have been dilated by long continued obstruction In this form of obstruction there may be a place for Duval's [6] ingenious technique for curing chronic relapsing pancreatitis [7] This condition is commonly thought to be due to obstruction at the sphincter of Oddi inducing biliary reflux into pancreas, but Duval doubts this and, believing that pancreatitis is caused solely by the obstruction and that biliary reflux is immaterial, he suggests that the pancreas be drained through its tail by transecting and implanting this into the open end of a Roux-en-Y jejunal loop He has successfully treated 2 patients in this way

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[1] Kirby C. K. Howard J M Rhoad J E. *Surg Gynec Obstet* 1955 100 158.
[2] Lium, R. Maddock, S *Surgery* 1948 24 593
[3] Millbourn, E *Acta chir scand* 1949 98 1
[4] Warren K W *J Amer med Ass* 1954 154 803
[5] Dunphy, J E. Brooks J R Achroyd, F *New Engl J Med* 1953 248 445

DIAPHRAGMATIC RUPTURE

THE diagnosis of traumatic hernia due to non penetrating injury is easily overlooked Most commonly the patient has received a crushing injury to the abdomen, so attention is directed more to possible visceral damage than to the abdominal parietes and chest Of the 7 cases seen by Evans and Simpson [8] 4 had fractures of the pelvis In the case reported by Dr Hamdi and Dr Sturdy elsewhere in this issue the patient appeared to have only a head injury, but while anæsthesia was being induced for reduction of a depressed fracture herniation took place through a diaphragm weakened by injury They agree with Evans and Simpson that a sudden explosive rise in intra-abdominal pressure, due to straining under the anæsthetic, can precipitate herniation This two stage mechanism—diaphragmatic trauma followed by herniation due to a momentary rise of pressure from below—can lead to further diagnostic difficulty since the two events may be separated by a considerable interval In 2 patients seen by Evans and Simpson six months and two years elapsed after the injury before the onset of symptoms, which in 1 case started quite suddenly while the patient was lifting heavy weights After such an interval the original injury may have been forgotten, and there may be no tell-tale scars to recall it Coincidental rupture of abdominal viscera is uncommon, and acute symptoms usually arise from displacement of lungs on the one hand and strangulation of abdominal viscera on the other In the case reported by Mr Sinha, also in this issue, the spleen was ruptured, but bleeding from it began only at emergency thoracotomy for reduction of the hernia Often, too, there is no pain referred to the shoulder, perhaps because the phrenic peritoneum is insufficiently irritated by a simple tear

Accordingly the diagnosis may be extremely difficult In a case lately investigated by a coroner [9] a young woman had received injuries to her face, body, and hip in a car crash After six days in hospital she was discharged, but returned almost immediately with internal hæmorrhage At laparotomy this was found to be due to recent rupture of the splenic vessels, the spleen itself was intact, lying within the abdomen, while stomach and colon had passed into the chest through a hernia in the diaphragm Radiography had revealed a diaphragmatic hernia which was regarded as congenital, and from the necropsy appearances it was concluded that the hernia was of long standing and probably congenital This may be another example of the double mechanism of a faulty diaphragm resulting later in expulsion of viscera into the chest

UNIVERSITY AND TOWN

FOR three days last month the University of Sheffie opened its doors to the people of the town Almost eve department in every faculty had prepared demonstratio illustrating the work they were doing In the faculty medicine, the department of medicine demonstrat the incidence of the killing diseases in a remarka cheerful way, and they allowed visitors to estimate th capacity of their lungs with a spirometer The departme of therapeutics and pharmacology showed some isoto techniques for measuring blood volume, and every could have an electrocardiogram while they wait Blood-transfusion work was vividly illustrated by th department of pathology, and the department of surgery had demonstrations dealing effectively with septic han arterial disease, and gastric acidity In the departme of obstetrics and gynæcology, the cycle of life, throu fertilisation, conception, and birth, was portrayed b *models and diagrams*

MEDICAL ASPECTS OF NUCLEAR RADIATON

THE membership of the committee on the medic *aspects of nuclear radiation* which, *as the Prime Minist* announced on March 29,[1] the Government invited th Medical Research Council to form, has now be announced The chairman is Sir Harold Himswort F R C P, F R S, secretary of the council, and the oth members are

Sir Ernest Rock Carling, F.R C S, F.R C P, consult adviser, Ministries of Health and Home Office (Civil Defen and member of the health policy committee of the Ato Energy Authority, Sir John Cockcroft, F.R S, director, Ato Energy Research Establishment, Prof Alexander Hadd M D, director, Chester Beatty Research Institute, J F Loutit, D M, *director*, M R C *Radiobiological* Research Un Kenneth Mather, D SC, F.R S, professor of genetics, Bir ingham University, W V Mayneord, D SC, professor physics applied to medicine, London University, P Medawar, D SC, F.R.S professor of zoology and compar anatomy, University College, London, J S Mitchell, M F.R S, professor of radiotherapeutics, Cambridge University L S Penrose, M.D, F.R S, Galton professor of eugen University College, London, Sir Edward Salisbury, D F R S, director, Royal Botanic Gardens, F G Spear, M deputy director, Strangeways Research Laboratory, Ca bridge, J R Squire, F.R C.P, professor of experiment pathology, Birmingham University, C H Waddingto SC D, F.R S, *professor of* animal genetics, Edinburgh U versity, Sir Lionel Whitby, F R.C.P, regius professor physic, Cambridge University, and B W Windeyer, F.R.C professor of radiology (therapeutic), London University

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[6] Duval M K *Ann Surg* 1954, 140, 775

[7] See *Lancet* 1954, ii, 1282

[8] Evans C J, Simpson, J A *Thorax*, 1950 5, 343

[9] *Wales Guardian*, March 18, 1955

[1] See *Lancet*, April 9 1955, p 768

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Special Articles

LEADERSHIP IN CARDIOLOGY*

The Charles Laubry Lecture

Sir JOHN PARKINSON

M.D Lond LL.D Glasg D.Sc N U I F.R C P
Hon. F.R C.P E Hon F.A C.P

In this lecture I am allowed to voice what is in my nd and memory In my mind is the realisation that e progress of cardiology has been mainly due to a ccession of individuals who proved to be leaders in ought in action and notably in discovery In my mory is the state of medicine, including cardiology en I began as a young student fifty years ago and the nsformation that has since taken place I propose to ak on three separate subjects first of those early ys and of that great leader James Mackenzie secondly specialism and the training of the cardiologist and rdly on French cardiology and the leadership of ofessor Laubry

Days Gone By

May I look back at medicine as I found it in my own ele at the London Hospital ? The study of the basic ences was limited to two years of inorganic chemistry ysics, and biology Then followed two years of atomy happily under Arthur Keith while physi gy was too largely a system of conflicting hypotheses, ough not for my own teacher Leonard Hill. All this ing over it was then our lot to live for as many hours possible with the sick in the wards and outpatient ics, learning by precept and practice what was ong with them and what to do for them We learned ly what our teachers knew except for what was in ir textbooks, the most popular of which was Osler's had no research consciousness though we were forced be clinically conscious In medicine our dozen teachers re equally chiefs ; but, looking back, how unalike their attitudes and talents ! Outstanding was Henry ad, an inspiring teacher but admittedly odd in having earch on the brain and even submitting to experi ntal operations on his own nerves Otherwise research d no place in the wards it was none of our business e were busy learning from our elders and there was a de variety of approach a wealth of practical experience those who moulded us One teacher one professor is ver enough the more the better—and often the rier Among them was that fountain of clinical sdom, Sir Robert Hutchison who is still with us and o prayed From inability to let well alone from much zeal for the new and contempt for what is old ; om putting knowledge before wisdom science before art, verness before common sense from treating patients cases ; and from making the cure of the disease re grievous than the endurance of the same : Good rd, deliver us'

During my medical apprenticeship our clinical practice s mostly empirical and we were not bothered by hniques As a clinical clerk I did use the first sphyg manometer in the hospital and a thin X ray film uld drift into the ward though it might show little yond the fingermarks of the radiographer There was n no separate science of psychology but patients were ted and treated as kindly as today though with less derstanding for the state of mind of the sick was not lised. Sex did not exist as a subject to be taken into ount by all doctors I had read Oliver Wendell Holmes however and he said ' The sound of a kiss is not so loud as that of a cannon but its echo lasts a great deal longer ' There were two kinds of heart disease, valvular and non valvular and we were satisfied Digitalis was given for heart failure in the wards but forbidden to outpatients Antibiotics were scarcely on the horizon and infections ran their course Many physicians had lost faith in therapeutics and patients were pacified with traditional remedies culled from the hospital pharmacopœia

In those last fifty years, medical practice has become more rational while advance by experiment has largely replaced advance by observation yet there is still ample scope in clinical science for patient observation I have been impressed by the way that the science of mind, psychology has gradually permeated practical medicine. Doctors more often and more exactly try to realise in their own minds the position and feelings of their patients. This studied humanism has largely taken the place of what was called the art of medicine Indeed today we may speak more simply and truly of the science of medicine It has been said that he is the best physician who inspires hope, but too often he brought ' no other medicine but only hope no material benefit Comparing the past with the present it is surely in *treatment* that advances of the greatest magnitude have been made The medical profession is greatly strengthened by the good will and moral support of the community and nothing has elevated medicine in public esteem more than the spectacular progress in medical and surgical treatment in recent years.

Men and Heroes

How then has medicine and with it cardiology, grown ? It is surely a story of men It is biography It is the life and achievement of a succession of men and women—a few of them geniuses many talented and a host with fewer gifts but determined to use them well Thus in a volume like Herrick's *Short History of Cardiology* we read a story of persons and their ideas and achievements rather than a summary of theoretical and factual progress.

In our boyhood and youth we all had our heroes bright and shining maybe historical or fictitious or martial but scarcely political and not at that time medical. As we emerged from boyhood and came to the study of Medicine this hero worship was still strong in us persisting through our medical training ; and many of our teachers became and remain our heroes You will agree that this faculty of admiration hero worship can and often does persist and that it still exerts a power in our lives It has truly been said that we are a part of all that we have met

People vary a great deal in the way they allow others to influence them Many are self sufficient sure of themselves independent Incidentally it has always been a surprise to me that Americans, whom the world regards as particularly independent and insubmissive to authority should be so devoted to their heroes—national social and medical Despite their inveterate fondness for something new and their urge to pursue the impossible they are catholic in their search for truth and love of learning Nowhere have the famous physicians of the past and of every country been held in greater honour than in the United States

Sir James Mackenzie

May I now remind you of the life and work of James Mackenzie the centenary of whose birth occurred last year ? At the age of 25 he joined a busy general practice in Burnley a Lancashire industrial town where, for twenty-eight years he practised medicine midwifery and some surgery It was under these conditions seemingly so unfavourable for such work, that the greater part of his original observations and researches was made Up to this time neither he himself nor others

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rom the Charles Laubry lecture delivered at the 2nd International Congress of Cardiology at Washington D C on Sept 17 1954 The full text appears in the May issue of *Circulation* published by the American Heart Association.

had much confidence in his powers or promise, his was a brain that developed slowly The stimulus proved to be the shock of realising his ignorance, his inability to understand or deal with the painful problems that faced him daily. One such was the unexpected death in childbirth of a woman under his care from heart failure He could not understand how or why it had happened or how it could have been recognised in time Such events stirred him to discontent, and so he consulted books and journals but found no satisfaction He did not know It did not seem to be known He would find out We cannot doubt that deep feeling has often been the spring of medical research It may thus depend on a man's upbringing and character, and his devotion to an ideal So Mackenzie set to work to study common symptoms like fatigue, dyspnœa, and pain, and to learn their significance by noting their clinical course over the years Impatient only with his lack of knowledge, he patiently took notes and made records year after year with a sphygmograph and later with the polygraph he devised but in which he took little pride Here was a genius for taking pains but a common sense that kept technique in its place as a servant and not a master

It had always been assumed that pain and tenderness arose directly from an organ, but Mackenzie gave the first description of hyperæsthetic skin areas associated with disease of particular viscera He showed that pain and tenderness were referred from an organ to the spinal sensory centres and thence projected to the periphery Such a "viscero sensory reflex" explained the curious extensions of pain in angina pectoris At the same time and independently, Henry Head was elaborating similar views which were published a few months after Mackenzie's

Herrick, whose death this year we lament, wrote "It was largely through Mackenzie's influence that the term 'heart failure' lost much of the opprobrium that had attached to it" Indeed it was not regarded as a proper subject for clinical investigation until Mackenzie convinced the world that the subject of heart failure was of paramount importance in heart disease, and its prevention and treatment the ultimate goal A similar revival of hope resulted from his teaching, based upon long observations on sinus arrhythmia, extrasystoles, and on murmurs which were compatible with good health In a clinical sense he isolated auricular fibrillation, at least in its relation to failure and to its particular response to digitalis

In 1902 appeared that remarkable book *The Study of the Pulse* which had no wide circulation but was quickly seized by the discerning as proof that a great investigator had been quietly at work for twenty years In 1908 came his *Diseases of the Heart*, and in 1909 *Symptoms and their Interpretation*, which together showed Mackenzie to be the most original and vigorous mind engaged in this sphere, and people began to talk of the "new" cardiology What was new was the critical, the scientific approach, and the introduction of hope into what had seemed so largely hopeless

In 1907 he had left general practice for consulting and hospital work in London In a few years he became physician to the Cardiac Department of the London Hospital, where he continued his researches and influenced the many physicians who came to his wards As years went by, he was limited physically by angina pectoris and in 1925 he died in London from cardiac infarction

What kind of man was Mackenzie to meet? He was Scottish in appearance and in accent, a massive figure with a slight stoop His bearded face, with its large brow, was carried by a large and noble head His eyes were searching, twinkling and friendly as his face was lit by a gentle smile, though not too often In general he was serious-minded and looked it, but there was a simple blunt humour near the surface Socially he was warm-hearted without being genial He was gentle in
dealings with patients, especially women, more
towards his assistants, yet appreciative Thus he
mightily pleased with his first resident, soon to be
in the first world war, who took better polygrams
he could himself

Though not by nature of a pugnacious temperam
he was a fighter for his opinions, and he had to be Th
was little appreciation and some opposition from ma
of the older physicians of his day I was warned of th
risks I took by becoming his chief assistant What
universal change there has been in the common atti
towards what is new, when it is true, and for this I
believe we have largely to thank the Americans!

Mackenzie, you will have gathered, found it hard to b
satisfied, yet it was a calm and hard headed man wh
carried that unquiet and inquiring mind More, he wa
a happy man, secretly gratified by his achievements an
their recognition, proud to have such friends as Cushny
Keith, Allbutt, Osler, Wenckebach, and Thomas Lew
and constantly sustained by the deep and abid
affection which existed between him and his wife

Specialism

The second of my three subjects is specialism and the
training of the cardiologist

Specialism has been called the growing point o
knowledge, and it is to specialism, disintegration in
sense, that the splendid advances of the last half-centu
have been mainly due Though many have opposed i
notice that no one has encouraged specialism, inde
that would be superfluous in so natural a process
remember well the time when medicine was held to be
indivisible, and cardiology was not regarded as
integral branch of it The word cardiologist was not
use, or it was used unkindly, whereas today a cardiolog
claims to be as truly a physician as any other The sto
criticism was that specialism engenders a narrowness
view, bad for the doctor himself and for his patie
But, as Hughlings Jackson said "There is no harm
studying a special subject, the harm is in doing
kind of work with a narrow aim and a narrow mind." I
cardiology, as in other branches, a new and broade
outlook has developed, it becomes more and mo
general The true specialist looks anywhere and every
where for the means of cure and prevention All th
physical, mental, and social factors relevant to his ow
subject are considered and integrated by him as the
never were before

In some quarters there are still attempts to for
trained and mature men to abide by the past custom
claiming acquaintance with the whole of general medici
But many young physicians are attracted by the wi
scope and variety of service which a special study of th
circulation and its diseases offers Medicine has divid
It already has children—the present specialties, an
now the grandchildren, the subdivisions—perhaps to b
future specialties—are growing up around us Norm
parents take pride in their offspring and are particul
tolerant towards their grandchildren The subdivi
or differentiation, which has come to pass in medic
as a whole, is now affecting us in cardiology An inst
is vascular disease, and the programme of our cong
proves the fact, for it is full of diverse subjects or
specialties

As a cardiologist, my personal attitude towards furt
specialisation can be simply stated Each individ
should be allowed to make his own choice, as he did w
he chose the profession itself Naturally he will seek
consider advice from his teachers though he is no
at school He may misjudge his own ability or the
for his particular endeavour, but he has a right to ch
the road he will take A wise man—and that could
a young man—should recognise his limitations, bu
must follow his bent The public is aware that

cular disease is predominant in human mortality
licine has always been influenced by public opinion
patients will surely claim the services not only of
eral cardiologists but also of special cardiologists who
e exceptional experience in one variety of circulatory
ease.

ining the Specialist

The serious danger of specialising too early is universally
nitted and it is effectively disallowed in our institu
ns But how long should the training in the sciences
l in general medicine be followed after graduation ?
re I suggest that for the future specialist it may
netimes be too prolonged ? Life is short For how
g should an ophthalmic surgeon restrict himself to
eral surgery and for how long should a young
rgeon remain in general surgery before concentrating
powers and gaining experience in cardiac surgery ?
nilarly a young physician—adequately trained as
ch—may prejudice the fullness of his career if he post
nes for too many years the plunge into what is to be his
e-work. So let us give greater individual choice as to
hich branch of medicine he favours and even, with the
feguards already mentioned as to what stage in his
reer he begins to specialise. I would hesitate more to
ake this unorthodox suggestion that specialisation may
gin too late if I did not know that there is often a
me-back, a natural return to greater commerce with
neral medicine as a man proceeds in his career

mpulsory Research ?

Happily there are plenty of men you cannot keep
om original research almost or actually bloodthirsty
their pursuit of it others only need putting on the
ent and they're off on 'the track of Truth" But
ust every ambitious graduate be forced by custom or
thority to prosecute research in order to obtain a
niversity post or to succeed as a practising cardiologist ?
esearch ability used to be regarded as a rare gift some
ing of a phenomenon. It was search with some prospect
f finding; it connoted both a spirit of curiosity and a
pacity for investigation That is not the attitude
day, though one must admit that it is largely the
pansion of organised research that has transformed
edical practice My question concerns the universality
f the capacity for research and I almost believe that
e true investigator great or small, is born not made
hat famous literary physician Sir Thomas Browne,
rote: "Every man is not a proper Champion for Truth
r fit to take up the Gauntlet in the cause of Verity'
ere is a matter of policy and procedure in our profession
hich will have to be decided. In my view we encourage
od men inapt for original research to sacrifice their
me and energy upon it when they should be perfecting
emselves as bedside physicians Are we losing our sense
proportion exhilarated by the wonderful products of
cent and current research ? Is a born investigator a
perior being to a born clinician and teacher ? He may
may not be Advances in medicine comprise two
parate stages: first the discovery of something new
d valuable as a result of investigation secondly the
plication of that new discovery to the benefit of the
dividual patient The same man may not be the right
e for both stages though he can be

Though commoner than aptitude for research the
wer to apply new (and old) knowledge judiciously is
t given to everyone It also requires a gift—namely
inical judgment This will ripen to clinical wisdom
ly by constant association with the sick Young
ysicians of this type—so badly wanted—need to keep
emselves abreast of the world literature in their
ecialty and devote time to postgraduate clinical work
other centres and in other lands Must they invariably
forced to shorten the time required for this large
rpose to participate in minor and often ephemeral
research before they are considered for any important staff appointment as a teacher or consultant ? Not every young physician or cardiologist should be under compulsion to prosecute individual research in order to succeed.

It would not be surprising if the magnitude and the magic of recent advances went to our heads The secret places of the heart are probed or rendered visible. The blood is directed where it may run and under orders when it may clot now even its channels are to be kept clear of their silt But after all scientific truth is discovered not created by us and knowledge is not always progress Some will remember the warning given by Professor Laubry at the European Congress of Cardiology in 1952 about the peril of technical dogmatism and the need to retain a measure of salutary doubt There is always a limit to scientific certainty in medicine, and some humility of approach is therefore becoming In fact, it is probable that we are producing both truth and error as our forbears have done The circus theory of auricular fibrillation for example seems to have come and gone but happily no patient has been allowed to suffer from this physiological disaster !

Research Applied

The original worker in research is fully aware of the importance of his subject and cannot be held back Are we as aware of the immediate importance of that other pressing duty that of applying the safest and soundest treatment to the sick of today ? I mean getting it applied more certainly and more universally If our minds are possessed by the greater things research will do for them in the problematical future, we may be less mindful of the *mass of human illness requiring our best endeavour* today The vision of new truth should not blind us to our bounden duty as doctors Any hospital may be proud of the amount of research being conducted within its walls But it should be equally proud of a reputation for applying—in current practice to the patients under its care—the sum of accumulated knowledge, the best treatment in the world today In this connection may I venture the opinion that the governing bodies of teaching hospitals would be wise to retain on their staff and value the services of an adequate number of practising physicians These should not be sacrificed at the altar either of science or of uniformity with loss to medical education and to the community *Indeed, a medical* staff will never be uniform, and the establishment should always be flexible enough to fit the exceptional individual and the late-developer and to take full advantage of any new perhaps unexpected, discovery

Unity and Friendship

I have touched on several problems for which, I doubt not solutions will be found or will naturally emerge Meanwhile we must be prepared for change willing to allow our younger gifted men freedom to strike out on their own lines according to personal inclination and judgment The call is to adapt ourselves to the changing form that cardiology is taking rather than to attempt to maintain its earlier compactness or to keep a strict symmetry in our organisation If only we cultivate the good feeling so evident at our congress we need have no fears for the future. Most of all the bond of unity will continue to lie in the grandeur of our purpose—namely the prevention relief, and cure of cardiovascular disease

When one speaks of unity and of leadership your thoughts will go at once to the president of our congress Dr Paul White Friendship for a country rests largely on personal friendships with its citizens. On that basis though not solely I would pay my *tribute to the lead* taken by the United States in the realm of cardiology and also give thanks for the close friendships which have bound me to this great country We spoke of hero worship, and Paul White remains one of my abiding heroes A counterpart to Osler in medicine, he has been an ambassador of good will and good hope to cardiologists all over the world He has made many original contributions, and by means of his famous book he has proved a trusty unseen consultant to countless doctors In it he has reverently combined a choice of the past with the best of the new

The French Contribution

Finally I want to say a little about the course of cardiology in France in recent years Following Potain there has been an unfailing sequence of distinguished cardiologists among French physicians First came pure clinicians like Merklen and Huchard, but it was the work of Vaquez, who combined the traditional French *clinique* with the physiological methods and researches of Marey and François Franck, that marked the beginning of contemporary French cardiology Apart from Laubry himself, to whose achievements I will return, we record with admiration the fine influence of Clerc, the brilliant observations of Gallavardin of Lyons in clinical cardiology, and the example of Giraud Then I would draw your attention to the constancy and the quality of the work of Professor Lian, a physician remarkable for his clinical discernment These have been followed, in strength, by Soulié, Lenègre, Froment, Heim de Balsac, Routier, and others

Inspired by the work of Helen Taussig and Blalock, and by their auspicious visit to Paris in 1947, Professor Donzelot and Professor d'Allaines, physician and surgeon, have combined in the last few years to make an important contribution from the cardiac centre at the hôpital Broussais This year, that work has been published by their brilliant co-workers, in particular Heim de Balsac, as a *Traité des maladies congénitales*, a large volume richly illustrated, and perfectly produced That is true also of another up to date French treatise for reading and reference, *Électrocardiographie clinique* by Lenègre and his colleagues

The contributions of France would be more widely evident today if it were not for the unfamiliarity of the English speaking countries with that graceful language We should all gain by a hearty understanding with France, a medical *entente cordiale* The place of France in the civilised and cultural world cannot be shaken by the passing effects of war or by political vicissitudes

Too often Paris has been solely a place for sightseeing and gaiety, and that was largely true in my own case On an early visit, however, I was privileged to go round the wards with the great Vaquez, who was attended most devotedly by his *chef de clinique*, no other than Laubry himself As Evan Bedford has said, " The great traditions of the Paris school of cardiology have been handed down in direct line from master to pupil for over a century, starting with Corvisart and passing in turn to Bouillaud, to Potain, to Vaquez, and finally to Laubry " Tradition may be a source of strength and a justification for authority To Laubry was bequeathed that authority and we realise today how valuable it has proved for the continuity of French cardiology under the trials of recent years Notice that he has been content to make this branch of medicine his life work, and the chair of clinical cardiology in the University of Paris was created for him

To begin with, he has been a brilliant clinical teacher, directly influencing students and graduates from the whole continent of Europe and elsewhere Lenègre has described those fascinating bedside clinics by the *patron* as reaching the unity and the charm of *a cardiological* ballet—though he allows that sometimes there might also be a display of fireworks !

Then since 1936 he has been the director of the *maladies du coeur*, founded by Vaquez in 1908 In the following year, he founded the Society of Cardiology Lastly, he has steadily tributed original research by way of clinical intuition synthesis combined with precise laboratory methods The work of his pupils bears testimony to his leadership and the important theses produced year after year under his direction indicate the scope of his interests and his capacity for guidance His son, Dr Pierre Laubry, has also made valuable contributions

Professor Laubry has methodically assembled his vast knowledge in book form In 1921, he published with Pezzi, a treatise on congenital heart disease In [illegible] appeared his famous *Leçons de séméiologie cardiovasculaire* and in 1930 his large textbook on heart disease One of his favourite subjects has been gallop rhythm, on which he wrote, with Pezzi, a valuable monograph Interested by Vaquez and Bordet in cardiac radiology, he instituted with Chaperon a long and painstaking research on the radiological anatomy of the heart and great vessels, normal and pathological, using radio-opaque injections The results appeared in two large volumes in 1939, *Radiologie clinique du coeur et des vaisseaux* by Laubry in collaboration with Cotte Routier, and Heim de Balsac It has provided a scientific basis for cardiovascular radiology, in particular, the composition of the vascular pedicle and the lung shadows was elucidated, and you will remember concept of the small aorta—large pulmonary artery 1950 appeared the second edition of *Les maladies coronaires* with Soulié, a comprehensive and modern textbook In the same year, to the amazement of those who had not appreciated the depth of his scholarship, for he carries his learning lightly, came his own translation into French of William Harvey's *De motu cordis* (1628) We in Britain especially value this tribute from one we are proud to number among the fellows of the Royal College of Physicians which the illustrious Harvey himself adorned

The outcome of a man's life may be measured by the ratio between his natural gifts and opportunities, and the service that he dedicates to the common good You will agree *that it is not only his talents but the* use he has made of them that has won for Professor Laubry the unique position in the cardiological world He possesses all the elements of greatness, and they are still manifest after an unusual experience in living, for he has passed his 80th year *In his long pilgrimage*, by teaching research, and personal example, he has set himself quicken and confirm progress in the wide realm of cardio-vascular disease, so that he has provided a veritable pattern of leadership

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PREVENTION OF JUVENILE DELINQUENCY

Two types of children come before the juvenile courts —mischievous young law breakers and unhappy problem children Sir BASIL HENRIQUES, who classified them this way when giving the Peter Le Neve Foster lecture at the Royal Society of Arts on April 27, finds the weakest part of child-welfare work in England to be preventive side

Many of the children born between 1939 and the of the war were separated for years from their parents and lived among strangers When the time came return, their mothers had become strangers and sometimes the children now had less liking for their mothers than for the foster-parents they now had to leave When their fathers came back from the Forces they too become strangers—*not only* to the children but times also to their mothers and the strangeness of parents to one another was as devastating to the children as their own strangeness to their parents Some of mothers had acquired new interests and did not welcome n back with the love and enthusiasm about which y had been long day-dreaming and some of the ers brought an almost military discipline into the ne, while some were over indulgent The war, in fact duced not only many problem children but many blem parents

The mischievous young law breakers Sir Basil finds ordinary boys with plenty of initiative and courage no proper outlets for their high spirits (This has n the experience of other observers: John Barron ys[1] noted that Liverpool boys often commit offences rely because they need to prove their courage to one other) Only some 46% of those committing crimes this country are detected, and every young delinquent urally expects to be among the 54% who are not ught Three things, Sir Basil suggested are needed prevent these crimes of adventure: first a police ce brought up to full strength and with better methods detection secondly enough playgrounds and sports unds for children and young people; and thirdly portunities for them to spend their leisure in a useful d constructive way He believes that the various youth ganisations could give them such opportunities, but at these organisations are chiefly handicapped by lack leaders of the right kind Pearl Jephcott,[2] however her study of membership of youth clubs found that ly about 1 in 3 children join clubs—and these are not cessarily the children who would profit most from em. Green spaces sports gymnasium and boxing ight attract more of those who now fail to join but at esent few youth organisations can offer all these things

THE UNHAPPY CHILD

But it is not in Sir Basil's view, the adventurous child much as the unhappy disturbed unsettled child who esents problems to the juvenile courts Lack of ordination between the various agencies dealing with prived and difficult children often results in failure to ke action as soon as anything amiss is noticed in child family He spoke warmly of the example of New South ales where every aspect of child welfare comes under e ministry which has concentrated on preventive rk Juvenile welfare in our own country is parcelled t among the Home Office and the Ministries of ucation Health and Labour

Abnormal behaviour in a child nearly always means at he is unhappy at home and many people have the ance to see his symptoms—the health visitor the rsing manager the staff of the nursery school or day rsery his teachers in his primary and his secondary hools the leader of his play centre his officers in the bs and Scouts his club leader the youth employment icer and (at every stage) his neighbours Some of se watchers are bound to realise when all is not well th him; but they are not clear what to do about it d often nothing gets done

He quoted the case of two little girls now aged 5 and 6 ose mother had died two years ago and whose father had en as his second wife a girl who had absconded from a ony of mental defectives Since there were now two rents to look after them the children (who had been in the e of the local authority) were sent home The teachers their school noticed that they lost weight and seemed ravously hungry and put them on school dinners. In the ter weather at the beginning of this year they came to school dly shod and in cotton frocks. They often said that they re frightened of their father and asked leave to keep their ts at school lest he should destroy them One afternoon y cried hysterically and refused to go home and their her called in the police and had them brought before the rt as in need of care and protection

Thirteen months earlier the health visitor had referred e case to the National Society for the Prevention of Cruelty to Children; and neighbours had also reported to the society that the children were never allowed to play in the street but were confined in a small back yard where there were rats If they were naughty they were put in a corner of the yard, and, if they moved the dog of which they were terrified was let loose

Sir Basil pointed out that the children's officer the school care committee, the education department and the after care officer for mental defectives (who was supervising the stepmother) all knew about this family yet these children had been allowed to suffer for many months without remedy

A CHILD WELFARE OFFICE ?

He suggests that we should establish in every town and in every district of cities, a child welfare office to which anyone concerned about the well being of a child can go for advice and guidance It should be a building worthy of its purpose presided over by the children's officer as director of child welfare and it should contain the headquarters of all the statutory and voluntary bodies which deal with the welfare of children This is no more dream, for in Manchester many of the voluntary agencies concerned with children already have their offices in the same house The juvenile court he thinks should hold its sessions in a room in the child welfare office—a suggestion which would not win the support of C A. Joyce headmaster of the Cotswold School, who believes that the juvenile court ought to impress the child, not give him the idea that whatever antisocial thing it was he did hardly matters. The great advantage of housing all the welfare agencies under one roof of course is that a family needing help can be referred at once to the appropriate body Thus parents persuaded to consult the probation officer could do so on the spot before their moderate ardour for his advice had time to cool

FAILURES IN PREVENTION

One great weakness in our present system Sir Basil thinks is the relatively slight attention we pay to absenteeism from school yet this is a sure sign of something wrong somewhere School inquiry officers are among the most poorly paid of local authority servants They should he suggests be highly trained family case workers employed not by the education but the children's department and it should be their job to discover the real reasons why the child is staying away—the negligence of the mother or her demands for the child's services in the home or the child's own failure at school which has led him to play truant Moreover if he was a trained child welfare officer teachers would tell him not only about absentees but about children sent to school dirty or persistently late children showing behaviour problems, and children, lately cheerful who have become sullen and morose

Sir Basil spoke of our failure to prevent some of those who leave borstals or approved schools from committing further delinquencies—blaming a system which reforms the child and sends him back to the unchanged home conditions under which he broke down 'Work on the family of a child or young person committed to a school or borstal,' he says, 'should commence the very day he enters the school. He proposes that all children under 15 who need residential training should be committed to the care of the local authority this would place the local authority *in loco parentis* until the young person reached 18 Approved schools for children under 15 would under this arrangement become members of a pool of ' residential schools ' ; and the local authority could send the child to the school appropriate to his needs—whether it was one specialising in delinquents or an ordinary school As no authority would wish to have more children in care than necessary, there would be an incentive, at present lacking, to get the home improved as quickly as possible This proposal has all the charm of orderliness, but it is hard to be sure that the irresponsible parents would really benefit from having their duties taken over by the local authority, or that the child would gain in security from learning that he was no longer under the control of his parents It is a situation calling for much careful thought

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[1] Growing Up in the City Liverpool 1954 See *Lancet* March 6 1954, p. 502
[2] Some Young People London, 1954 See also *Lancet loc cit.*

A MINISTRY OF JUVENILE WELFARE?

Finally Sir Basil would like to see the children's department of the Home Office, the Ministry of Education, the National Youth Employment Council of the Ministry of Labour, and the department of the Ministry of Health which deals with children of school age and under, combined to form a Ministry of Juvenile Welfare, a minister of Cabinet rank This idea too has attractio its weakness is that it separates the child's situation that of the family as a whole—and this, as we are and painfully learning, cannot be done Perhaps one towards a coordination of services is to begin at the end, as the *Times* (April 28) suggests, by training a set of "general-practitioner" family case workers replace the multiplicity of inquiring people now visiting the homes of families with problems Like her counterp in general medical practice, she would be able to ca just the agencies which could help, thus coordinat their efforts from the start.

Public Health

THE POLIOMYELITIS-VACCINE CONTROVERSY

FROM AN AMERICAN CORRESPONDENT

THE announcement on Franklin D Roosevelt's birthday of the effectiveness of the Salk vaccine in protecting against poliomyelitis was greeted in the United States with great satisfaction both by the lay public and by the medical world Since then there has been a tremendous hullabaloo which has been and is being stoked up by the press, radio, television, and the Poliomyelitis Foundation For one thing, there has been an argument about the distribution and use of the vaccine, and this has been engaging the attention of the United States legislative bodies, organised medicine, the trade unions, and the pharmaceutical houses The public want the vaccine "for free" (as they say) they have contributed generously year after year to the March of Dimes fund of the Poliomyelitis Foundation and they feel that they have bought their share of this advance On the other hand, the pharmaceutical firms need to recover their investments and wish to make a profit for their stockholders, while doctors, with no national health service behind them, quite properly want to charge for giving the injections

Much more disturbing was the announcement that poliomyelitis had developed in a number of children who had had vaccine prepared by the Cutter Laboratories, and this vaccine was withdrawn from general use While the facts and the possible explanations have been presented at length in the press, a much quieter scientific controversy was going on, and this has been brought into the limelight at the annual meetings of the American Society for Clinical Investigation and the Association of American Physicians which were held last week at Atlantic City Dr Jonas Salk and Dr Albert Sabin have long held opposing views about vaccination against poliomyelitis For many years they have presented their hypotheses at medical meetings, but this year they came up with facts, and it looks as though Sabin may be right He favours the use of attenuated-virus vaccine given by the natural route of infection (by mouth), while Salk believes that formaldehyde killed viruses given parenterally will produce antibodies as effectively as and more safely than modified living viruses Sabin has contended that intramuscular injections of killed vaccine will not confer lifelong immunity and that it would be impracticable to re vaccinate each time the short lived artificial immunity runs out If children received such a short term vaccine, he argues, there would soon be a population of young adults with no protection against poliomyelitis, and as the disease is more severe in adults than in children, a vaccine which confers only a short immunity might eventually result in many severe illnesses when the children grew up This situation is already developing for a different reason in the United States Great Britain, for example, where standards of hyg are high and natural infection is therefore relativ uncommon The exact duration of immunity confe by the formalin killed vaccine cannot yet be known. Salk has suggested, on the basis of studies on a lim number of subjects, that the immunity will be life-long

Salk's short paper given at the annual meeting of American Society for Clinical Investigation was his presentation of data collected from last year's huge test of the action of polyvalent vaccine in produ *antibody in children* *Three serial injections* were g and antibody titres were measured at frequent inter before, during, and after the vaccinations The first vaccinations were given close together, and the th or "booster" injection a variable time later Sal found that the immunological response to poliomye virus antigen in man was made evident by two measur reactions—the antibody response itself and the sta hyper reactivity to subsequent antigenic stimulation. *the hyper reactive state there was a shorter* inte between provocation and secondary antibody resp and the secondary response was very *much greater* th the primary one The degree of the secondary resp was shown to be influenced by the intensity of prim stimulation, the intensity of the secondary stimula and especially by the interval between primary secondary stimulation The full secondary effect in could not be elicited unless the secondary stimula was given several *months after the primary* inject These factors were also found to influence the degre which the serum antibody *levels tended* to pe Immunological response in man, following injection non-infectious poliomyelitis virus vaccine, was affe by previous immunological experience with one or of the three types of viruses, responses being striking with previous exposure to type III virus. also suggested that the presence of *measurable* amo of circulating antibody in children *may not* be an essen prerequisite for immunity to paralysis In some chil no antibodies were found in the blood, yet they respo to the primary injection by a rapid rise in antibo which persisted in the blood *It seemed clear* that t children had been previously exposed to natural p myelitis without getting paralytic disease Salk s lated that the hyper reactive state was an impor protective mechanism against natural poliomyelitis believed, on the basis of this work, that natural rea tions with poliomyelitis after invasion through natural portal of entry, will stimulate promptly formation of antibody and thereby limit deeper inva *or further multiplication* of the virus The ex question of life-long immunity could not be answ at present

Sabin, who is director of the research unit of Children's Hospital of the University of Cinc Medical School, presented his investigations to the A ciation of American Physicians He has deve mutant attenuated strains of virus which, when g chimpanzees by the natural oral route provoked the velopment of antibodies in the circulating blood and nferred 'life long' immunity to the three types of ralytic poliomyelitis virus The chimpanzees had no ognisable illness as a result of exposure to the atten ated virus and these viruses have never reversed their tations to reappear in the virulent paralytic form for the chimpanzees Sabin described a dramatic experiment ith 26 young volunteers in the Federal reformatory at illicothe, Ohio Varying doses of living attenuated us were given to the men in a drink of milk and tibody titre was measured serially Repeated cultures re collected from the mouth throat and fæces tibody formed rapidly, and has so far persisted in e blood Virus could not be recovered from the mouth, it was recovered from the throat and fæces With ge doses of virus the stools have remained positive up to three months The minimal dosage was 001 ml of the pure culture This amount of virus voked excellent antibody response when swabbed on e throat of the volunteers. No illness appeared in any the volunteers nor in the men who were in close ntact with them in the reformatory Sabin stated at when comparative studies had indicated the best ains to use, it would be *possible to determine* whether not the optimum attenuated poliomyelitis virus—her given in milk or simply swabbed on the throat—uld be used for primary immunisation or for production an effective type of immunity in individuals temporarily tected by natural antibody or non infective vaccine

It was clear that many doctors at the meetings feared t the public had been too readily convinced that liomyelitis had been conquered For there are many ering facts for example quite apart from any ention of infective batches of vaccine many vaccinated ldren will get poliomyelitis for the Francis report de no higher claim than that the vaccine was effective 60–90% of those who received it

Issue of American Vaccine Suspended

Further supplies of poliomyelitis vaccine will not be ued in the United States until an inquiry into manu turing standards and safety tests has been completed nouncing this on May 6 the Federal Surgeon General, Leonard Scheele said that the vaccine was still ing produced but Federal approval of additional pplies was being held up for several days.[1] Scheele was testifying before the banking committee the House of Representatives on pending bills that uld give the government power to control the price d distribution of the vaccine. He was confident that experts now examining the situation would conclude at the vaccine was excellent and that vaccinations ould go on It would be decided in the next few days ether the vaccine would continue to be tested by spot ecks as at present or whether every lot should be amined Dr Scheele said that on May 6 the total cases of poliomyelitis in newly vaccinated children 11 of whom 38 had been given Cutter vaccine ked whether this vaccine was now suspected he lied: We have to have a lot more evidence before could decide[2] Since April 1 he said there had en 384 cases of poliomyelitis in the United States, mpared with 423 in the same period last year

In a report issued two days later Dr Scheele announced at a detailed reappraisal of each lot of vaccine already pared or in final stages of production was being dertaken[3] He hoped that vaccine would be available use again by the end of this week There had been cases of poliomyelitis among more than 5 million ople vaccinated, and if only 1 in almost 700 000 ldren inoculated with vaccine from companies other an Cutter Laboratories had incurred paralytic polio-yelitis Dr Scheele added this meant there was every ason to believe a product of the other manufacturers is safe He said there was a definite association between the Cutter vaccine and the cases of poliomyelitis that had developed after its use So until the precise cause was found the vaccine produced by this laboratory would remain suspended

The Medical Research Council has sent a member of its staff to the United States to obtain first-hand information. This should be available before the routine safety tests on the present batches of vaccine are completed and therefore, before any proposed trial in this country is due to begin Meanwhile, the council will continue with the arrangements for starting the trials.

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[1] Times May 7 1955
[2] New York Times May 7 1955
[3] Times May 9 1955

Cadmium Poisoning

The industrial diseases subcommittee of the Industrial Injuries Advisory Council is considering whether cadmium poisoning should be a prescribed disease under the National Insurance (Industrial Injuries) Acts, and if so for what occupations. Industrial injuries benefit can already be claimed for acute cadmium poisoning as injury by accident. The committee are inquiring into the possibility that prolonged exposure to cadmium at work can give rise to chronic ill health against which insurance cover should be provided Persons and organisations interested in the question of prescribing cadmium poisoning are invited to submit written evidence Communications should be addressed to the secretary, Industrial Injuries Advisory Council, 10, John Adam Street London, W C.2 to arrive not later than June 6, 1955

Infectious Diseases in England and Wales

Disease	Week ended April				
	2	9	16	23	30
Diphtheria	8	5	7	14	9
Dysentery	1809	1467	1191	1053	879
Encephalitis:					
Infective	4	4	6	3	3
Postinfectious	4	2	5	0	3
Food poisoning	156	180	158	135	177
Measles excluding rubella	33,324	[illegible]0,885	32 980	28 474	22 537
Meningococcal infection	11	30	*8	36	38
Ophthalmia neonatorum	13	46	30	48	44
Paratyphoid fever	17	13	2	15	15
Pneumonia primary or influenzal	1050	872	804	688	510
Poliomyelitis					
Paralytic	5	2	14	1	0
Non paralytic	1	4	0	5	10
Puerperal pyrexia	224	213	*53	220	270
Scarlet fever	524	666	507	107	461
Smallpox					
Tuberculosis					
Respiratory	704	614	609	88	867
Meninges and C.N.S.	13	14	17	21	20
Other	65	61	50	76	80
Typhoid fever	2	4	*	3	
Whooping-cough	1842	1310	1471	1664	1703

* Not including late returns

Medicine and the Law

State of Doctors' Surgeries

Two decisions by the London Executive Council at its meeting on April 28 concerned the duty of practitioners under the National Health Service to provide and to permit the inspection of proper surgery accommodation Clause 7 (4) of the Terms of Service requires the practitioner 'to provide proper and sufficient surgery and waiting room accommodation for his patients having regard to the circumstances of his practice Clause 7 (5) provides that on receipt of a written request the practitioner shall at all reasonable times admit any member or officer of the council or the local medical committee authorised by the council for the purpose of inspecting the surgery or waiting room.

In the case of Dr A an inspection was made in February, 1955

Dr A's surgery hours were from 11 A.M. to noon but when the inspecting officer called at 11 40 A.M., Dr A who apparently slept in the consulting-room was not ready to receive patients In the waiting room was a quantity of old paper, a dilapidated leather trunk and a tin box The consulting room was in a state of muddle The floors had no covering and had not been swept The visit was paid when there was snow on the ground, but there was no evidence of a fire in the waiting room, although Dr A said that a fire was provided when required There was no running water in the consulting room and no light in the lamp holder in the waiting room, and in both rooms the windows and curtains were dirty

Dr A was invited to submit observations and to attend a meeting of the medical service committee He failed to do either The executive council adopted a recommendation that representations should be made to the N H S tribunal that the continued inclusion of the practitioner in the council's medical list would be prejudicial to the efficiency of the service

The case will now be subject to inquiry by the tribunal

In the case of Dr B the local medical committee had asked for an inspection of the surgery and authority had been given by the chairman of the council

Dr B agreed to receive the inspecting officers and the hearing was fixed for March 11, 1955 Dr B subsequently wrote stating that the date was inconvenient as decorations to the premises had not been completed and the council to defer the inspection until the middle of The council replied that they had not asked that the should be re decorated before inspection. Dr B was that the duty of the inspecting officers was to report to council on the present condition of the premises and that information he gave as to re decoration &c, would incorporated in the report The apparent reluctance of doctor to permit the inspection of the premises was to the notice of the appropriate committee on March and on the following day the doctor was notified that committee had decided to refer the matter to the service committee unless he indicated several days the ensuing fortnight on which the surgery could inspected No reply was received from Dr B

The medical service committee considered that had shown a complete disregard of his obligations the Terms of Service and they advised that a mendation be made to the Minister of Health the sum of 30 guineas be withheld from his remuner The executive council adopted this recommend which is subject to appeal

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Parliament

Review of Social Services

In the House of Commons on May 4 Dr Edith Summerskill, in opening a debate on the social services, regretted that the report of the Phillips Committee on the economic and financial problems of the provision for old age, had been ignored by the Government She pointed out that the new scales would not help the old-age pensioners on National Assistance Of those on sickness benefit 123,000 would only get 2s 6d extra, and most of the people receiving this benefit were the chronic sick This led her to ask the Minister of Health if he was satisfied that, having regard to the hardship it imposed, and the administrative burden it entailed, the shilling prescription charge should be continued? Had the Minister inquired in districts where industrial processes had a deleterious effect on the workers' teeth to see whether withholding a free service had resulted in a deterioration of dental health? She understood that £50 million was spent annually on drugs, 30% of which went on proprietary drugs She found it difficult to understand how the Minister could allow this huge sum to go on swelling the large profits of the big drug houses, knowing how cheeseparing he was in other directions The Minister had been trying to persuade doctors to use cheaper alternatives, but he had done everything except take strong action He should refuse to sanction unnecessary expense in prescribing when there was a satisfactory alternative

Mr Iain Macleod interposed that Dr Summerskill's suggestion might infringe the right of a professional man to decide what, in his judgment, was best for his patient Though advice had been given to doctors that certain drugs were not of proven therapeutic value, if a doctor in his own discretion still decided to prescribe one of them it was perfectly legitimate for him so to do

Dr Summerskill went on to ask if the Minister thought he was justified in allowing hospital beds to be earmarked for fee-paying patients when in some districts there were long waiting-lists, and whether he could report any improvement of conditions in our mental hospitals

Mr Osbert Peake, Minister of Pensions and National Insurance, described the Phillips report as "most valuable" and said that it was clear that as a result of it there would have to be legislation at a later date amending the National Insurance scheme But he thought the scheme was a good one and he would be reluctant to introduce changes into it just for the sake of changes He had been assured by the National Assistance Board that the increases in February had fully restored the loss of purchasing-power of the allowances which had occurred since June, 1952 In July, 1948, the Assistance Board were paying 842,000 allowances, that figure had risen by the end of March, 1955, to 1,807,000 increases in pensions would reduce by 100,000 the num going for assistance

Mr Kenneth Robinson returned to the case of boy with a fractured and dislocated arm who had at Hampstead General Hospital for more than six before he received medical attention Mr Rob had found the Minister's reply about this case satisfactory[1] But the matron immediately began give interviews to Press reporters in which she said she had not heard of anyone being reprimanded explained that the boy had been kept waiting for hours because it had been impossible to get a spec in the hospital sooner, and that he had not been food or a sedative because he was to have an anaesth Mr Robinson shared the great respect and gratitude the House and the country had for the nursing profe but it seemed to him that some members in the ranks of the profession were rather resentful of critic The matron of this hospital had in effect repudiated Minister's apology and Mr Robinson felt that the could not be left there

Mr Macleod agreed that Mr Robinson was to raise this case in the first instance and, in view of statements which had been made, he was wholly rig raise it again He, like Mr Robinson, had hoped with the full apology which he had made on behalf the board of governors, and in particular on of the Hampstead General Hospital, the matter had closed He had been considerably startled to read in newspapers the comments which the matron had The answer which he had given to the House on was made after consultation with the board of gov and it had the agreement and encouragement of people responsible From time to time one got impression that the people concerned in these were a little reluctant to admit that they were in because they thought that might reflect upon a h of which they were rightly proud In his view that a wrong attitude If a fault was found, nothing hospital more credit than to say that it was wr and it was right that an explanation should be frankly to the House of Commons by the Min responsible, as had been done in this case Be hospital had slipped in one particular instance, it did mean that it was not a fine hospital with fine as he was quite certain was the case here We all ad the quality of loyalty and he could easily under a matron who was proud of her hospital and the working there resenting, perhaps a little too any suggestion that the hospital had slipped in its But what had been said was unwise and unf it should not have been said, and he was certain that matron much regretted having made an allegation he understood she had—against Mr Robinson himself urning to the question of prescribing Mr Macleod that it was entirely within a doctor's discretion to scribe a particular drug even though it had been gested by the committee and Ministry that this was advisable He would not be surcharged for that as possible—and this was a different point—that his scribing as a whole might be looked at, and one element ght be the over-prescribing of one particular drug Macleod did not see how they could achieve what Summerskill seemed to have in mind which was ited to the prescribing of the ordinary substances the list without interfering with the ordinary clinical edom of doctors He would not wish in any way to erfere with the right of a doctor to prescribe at his cretion in individual cases The total bill for England d Wales for medicines was about £43 million not luding hospitals, and within that sum £21 million a little more than half was due to proprietary medies. That was cost alone the non proprietary preiptions would be more than half because the others re more expensive Many of the greatest discoveries, h as the antibiotics, had been made by private firms garding the pattern of dental treatment, Mr Macleod d that the important fact was that conservative atments had gone up from 4 070 000 in 1951 to 00,000 in 1954 that in the school dental service the mbers, which had fallen at the end of 1951 to 713, d risen at the end of last year to 979 The dental atment of the priority classes was a great deal better n it had ever been

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[1] See *Lancet*, May 7, 1955, p 966

About 1% of the beds in the National Health Service re private beds and about a third of those at any given e were occupied by non-paying patients, either on unds of medical urgency or to see that the beds were ed The proposal to abolish pay beds was a breach faith with millions of people who paid into contributory emes so that they might have some privacy in spital.

The mental hospitals had no waiting list, and the 8500 ls that were being provided were a contribution to the ief of overcrowding For the mental-deficiency spitals there was a waiting list of about 7000 5007 ls had been completed, or were nearly complete, d there were also 915 beds included in the 1953–54 gramme, not all of which could be actually occupied There was therefore a programme of at least 00 beds as against a waiting list of something like 00 But the Government had recently announced substantial hospital building programme and the ntal-deficiency side would get its full share

Prison Reform

In the House of Lords on May 4 Lord PAKENHAM in ling attention to the Prison Commissioners report for 53 said that he had lately shared in an inquiry, under en on behalf of the Nuffield Foundation into the es of crime, and in the last year or two he had ited some 20 prisons or borstals. He submitted that xt to nothing was being done to reform the majority convicted prisoners indeed it might well be argued at they were likely to come out of prison worse than en they went in We were not making an effort in s direction commensurate with our degree of social lightenment in other fields

The overcrowding of our prisons—the fact for instance, at out of 17 485 in prison 2880 were still sleeping three a cell—was a sore impediment to the best intentioned ison staffs. The most troublesome bottleneck which day frustrated the efforts of all who would like to extend e training system using that word in the sense not ly of trade training but also of moral training was e shortage of staff Today the three-shift system was force in only a quarter of our prisons But without the idea of individual treatment for prisoners would main a fantasy It was a major and imperative duty ther to bring down sharply the number of prisoners to increase rapidly the number of staff

Viscount TEMPLEWOOD pointed out that only 21 000 en and women were involved Surely a welfare State th all the immense improvement that we had seen in ery social service could deal with this small problem an urgent and common-sense manner Yet instead of progressing, so far as accommodation and work went we had fallen back 50 or 60 years. He urged that there should be an inquiry into all prisoners records to see how many of them could be allowed to work outside prison Work in prison should be useful and paid for at regular rates. The money should be allocated to the man's keep, compensation for the victims, and the provision of a sum for the prisoner when he left prison The best hope for many offenders was to make them work and make them take an interest in it Lord MOYNIHAN suggested that there should be compulsory aftercare for boys of 14–17 who were sent to detention centres He would like to see the system of ' home leave extended and given not only to those who had happy homes but also to the homeless He was sure that carefully selected families would be prepared to take these boys in the first weeks of their probation The appointment of permanent welfare officers in prisons would be a great step forward

Lord MANCROFT, joint parliamentary under-secretary of State for Home Affairs, said that the prison and borstal population in 1930 was 10 000 and by 1952 at the peak it had reached 24 000 Since then it had gradually decreased and was today about 21,000 The effect of the sharp rise was that in 1952 there were 5200 prisoners sleeping three in a cell That figure was now down to 3000 Nothing but necessity excused that deplorable state of affairs Oddly enough, this situation had had little effect on health and discipline, but it remained wholly undesirable Overcrowding was not allowed to interfere with training in specialised prisons; its effects had been confined to local prisons. The plans for new prisons were based on the bold decision to break away from the traditional walled prison and to place in open conditions all who could safely and properly be trained there. There was no shortage of men coming forward for posts as prison officers, but they were not always the right men Recruits were urgently needed There had been a shortage of work in the prisons, but the past year had shown improvement In all specialised training prisons there was a full working day in good class industrial work. The treatment of prisoners was now dominated by the conception of training The Government stood by that conception and believed it to be wholly right and proper

Full use was being made of the detention centres by the Courts, and it was hoped to widen the system The centres were making an effective contribution in combating juvenile delinquency Many prisoners who had otherwise been written off as hopeless had been saved from a life of crime by flexible methods of corrective training Greatly increased medical services had been set in progress since the war in local prisons, directed towards rehabilitation—particularly psychological and psychiatric services rehabilitative surgery and specialised treatment under the National Health Service, both in outside clinics and in hospitals While there was still great room for improvement there had been a great effort to improve the Victorian sanitary conditions in prisons and this effort would be continued The whole process of aftercare for prisoners other than in local prisons, had been reorganised by the formation of a Central After-Care Association, and by the decision to bring in the probation officers as field workers for the association Every prisoner in the care of the association after his release was under the immediate supervision of a skilled social case-worker

QUESTION TIME

Review of Extraction rates of Flour

Replying to a question Mr HEATHCOAT AMORY Minister of Agriculture and Food said that he had decided in conjunction with the Secretary of State for Scotland and the Minister of Health to arrange for an independent authoritative review of the scientific and medical evidence now available in regard to this matter Lord Adrian president of the Royal Society had nominated for the conduct of this review the following panel of representatives of scientific and medical opinion:

Sir Henry Cohen F.R.C.P. professor of medicine University of Liverpool (chairman) L J Witts F.R.C.P., professor of clinical medicine, University of Oxford J H Gaddum, SC D, M R C S F R.S, professor of materia medica University of Edinburgh A C Chibnall SC D F R.S, formerly professor of biochemistry, University of Cambridge R A Morton D SC., F R.S professor of biochemistry, University of Liverpool

The terms of reference of the panel are

In the light of the scientific and medical evidence now available to determine the differences in composition and nutritive value between (*a*) National flour as defined in the Flour Order 1953, (*b*) flour of extraction rates less than National flour as defined in the Flour Order 1953, to which the three token nutrients have been restored (*c*) flour of extraction rates less than National flour as defined in the Flour Order 1953, to which the three token nutrients have not been restored and to advise whether any such differences are significant from the point of view of the health of the population

Poliomyelitis Vaccine

Replying to a question, Mr J R BEVINS, as representing the Lord President of the Council, said that the current programme of poliomyelitis research coördinated by the Medical Research Council might show whether there was any practicable alternative to the use of monkeys in preparing a poliomyelitis vaccine, but he was advised that an adequate substitute for monkeys was unlikely to be found in the near future for a vaccine of the Salk type It was hoped, however, that adequate supplies of monkeys would be available again shortly He could give an assurance that research to find a promising substitute was going on Before any of this type of vaccine was used in this country it would be very carefully tested on monkeys or some other animal

Replying to a further question, Mr MACLEOD said that recently reported events in America were being fully considered by the M R C, and a member of their staff was going over there immediately to get first hand information This should be ready for study here before the routine safety tests, now being conducted on batches of vaccine, were finished and therefore before any of the proposed trials on children over here were due to begin Meanwhile arrangements for these trials continued There was no intention of inoculating any child unless the full consent of the parents had been first obtained

Postal Votes

Replying to a question, Mr IAIN MACLEOD said that he had studied carefully the documents sent to him about pressure being brought to bear on doctors by local Conservative associations to send them the names and addresses of their sick, blind, and aged patients for the purposes of the postal vote It was desirable that everybody should be aware of their right to a postal vote and equally important that any information given should be made available to all political parties who asked for it There was nothing wrong in responsible citizens, doctors or others, bringing to the notice of those concerned, whatever their politics, their rights as postal voters On the specific question about extracting patients' names from doctors' lists, he would not expect information concerning doctors' National Health Service patients, which was normally regarded as confidential, to be disclosed for some entirely different purpose He was sure that doctors understood the position and that no special communication was necessary

Welfare Foods

Replying to a question, Miss PATRICIA HORNSBY SMITH gave the following figures for the distribution of welfare foods

Welfare food	1953 July–Dec	1954 Jan –June	1954 July–Dec
National dried milk (millions of tins)	12 34	11 92	11 33
Cod liver oil (millions of bottles)	3 28	3 30	2 79
Vitamins A and D (millions of packets)	1 03	1 03	0 83
Orange juice (millions of bottles)	15 58	14 81	13 41

These foods, she added, were intended for those whose diet might otherwise be deficient, and the arrangements of the local authorities were well adapted to concentrate attention on this group In the community as a whole the downward trend might well continue with the continuing improvement in the general diet and standard of living The department would maintain a close watch on developments

In England Now

A Running Commentary by Peripatetic Correspon

To conduct, control, and conclude a consultati a querulous, persistent patient is an exercise in ap personality that can be fascinating to the be although arousing different emotions in the p Medical students may study their chiefs and in outpatient departments the patients may fill their waiting time by making extensive observations on the subject I have had the good fortune to pursu subject *under both conditions and here* pres preliminary report

The commonest method, and one lacking all ch to terminate the interview and stop all further que is " I'll write to your doctor You go round and disc it with him next week " The psychiatrist, and those of psychiatric leanings have an altogether more diplom approach, an approach designed to act like foam o fire, to damp down and smother the burning pass and to allow those that will not be smothered to b themselves out These experts just let the pati on talking and talking while they remain emotio impassive, impersonal, and aloof At the end of allotted hour they quietly make an appointment fo further instalment, no doubt noting in their notes " Next Week " Another subtle, though somewhat approach is to appeal to the patient's self-esteem by *flattery This is often successful with readers of pop* medicine articles You merely have to preface y remarks with " A man with your knowledge of medi will at once realise " Another convenient for for the rushed doctor, but one liable to cause addict and even abuse by the lazy, is the " Let-me-know gets-any-worse " approach This is of course not f proof, for next week the patient may return to that it has become worse Under such conditions ano line must be taken. One may assure the patient t he has a very rare, interesting complaint for which yet there is no treatment (this is much favoured neurologists), one may keep them under observat (a physician's gambit), or one may adopt the " Th funny, *I have the same trouble myself*," and th unload your anxieties and symptoms upon the pat Oddly enough this seems to help both the patient *the doctor*

* * *

We are once again in the midst of an election batt with all parties in search of the elusive floating v and I am irresistably reminded of the last electi and Annie

Annie was one of several hundred old dears a home for the aged Never very active, she was confined to bed permanently with gangrene of foot, which she stubbornly refused to submit to surg She lay there in gloomy silence, and appeared to abandoned all interest in life

Which party it was, I forget, but some shrewd poli type saw in the home a happy hunting-ground for A fleet of cars arrived, and all those passed as " were taken to the poll. Annie pleaded for a ride, I hadn't the heart to refuse

On her return she was in a state of considerable tion " I do hope I done right—I suppose it's all for best " The old dear commented so seldom upon thing that such concern over the election was ext ordinary Sister investigated Annie was quite sure had just given consent for her leg to be amputated

I often wonder for whom she voted

* * *

As our taxi hurtled over the perilous track to Bab we found the driver glad to talk of life in his count We passed a convoy of army trucks given by the Un States and mobile A A guns made in England, then army camp Oh yes, there was national service, he s two years for all men—unless they paid 50 dinar which case it was three months That is official dinars secures complete exemption That is unoffi We skidded and slid in the sand, bumped, and th our way from one mud hollow to the next, and s smiled and joked. There was the way trucks are overloaded (nearly everyone we saw was an example) —When the last bus home was full the driver sent his colleague on to the roof among the luggage. But that night it was windy and cold so he shared a coffin with its rightful owner on his way to his burial When the next man came up on the roof the living occupant of the coffin put out his hand to show he was there He went to court—not for travelling with a corpse in a coffin but for putting out his hand in such a way as to frighten the newcomer Three months jail was the price of his thoughtlessness.

"We are living in the 10th century here our driver said as our 20th-century limousine survived mile after mile of insult. Wives are still cheap 50 dinars buys the ordinary kind 100 the very best If the husband does not like her he kills her She was no good ' in the law courts means no worse a penalty than two months in prison That is the law, you see." What happens if a man murders another man? we asked Oh he is hanged of course," he replied

Wives do the work while husbands sit in the cafés smoking their great ' hubble-bubble ' pipes. Toiling in the fields on either side of us through the hours of light were these poor peasant women heavily clothed in tattered black. There, too, were superb birds feeding in freedom Large green bee-eaters swooped on flying insects blackwinged stilts probed the saltings with their graceful bills a solitary flamingo stood still. 'If I d had the chance before I was born to choose what to be, I d be a bird, he said I see what he meant.

* * *

My peripatetic colleague surely cannot seriously intend that we should instruct our adult patients to Lie on the couch with your tummy upwards.' But I agree that the usual ' Lie on your back on the couch ' regularly results in a patient lying on his face The remedy came to me in a moment of inspiration: 'Lie down on the couch please. I say no more no less I have yet to see a patient who spontaneously adopts any but the supine position

* * *

Last year our rural district almanack and directory had some interesting health notes and hints for the nursery

" Headaches, dizziness and shortness of breath are often caused through neglecting the feet

"Cramp generally arises from a disordered liver For quick relief from the pain the feet should be plunged into hot water and rubbed hard with a towel. If hot water is not obtainable rub in camphor liniment or embrocation.

"If a person cannot sleep it is because blood is in the brain; the remedy therefore is to draw blood down from the head. This may be done by eating one or two small onions or a biscuit

"It is harmful to force a baby to take notice The brain will develop much better if left naturally

"Paddling in the sea is a serious danger to many children. Paddling has been known to cause convulsions, cramp heatstroke and severe bronchitis

Unfortunately the publisher seems to have had a hint that the notes are a little outdated for this year they have been replaced by notes on bird life and a page of wit and humour

* * *

In bed with another overpowering cold I am feverishly wondering why this type of coryza major never afflicted me until I came to British Columbia But here of course the forest trees are enormous, the buttercups grow twice as high as those in English meadows, and gigantic salmon throng the rivers. I ought to have known that the viruses would be jumbo size

* * *

Psychiatrists must look to their laurels, for it seems that their closed shop is not so closed as they think. In the last issue of *The Lancet* I read of kidneys showing "a diffuse distal tubular neurosis Imagination boggles at the future Are we to hear of neurotic syndromes relating to all histologically differentiated regions of the body? Sorry Old Man can't play golf today, I've neurosis of my islets of Langerhans

Letters to the Editor

BLOOD-AMMONIUM LEVELS IN LIVER DISEASE AND "HEPATIC COMA"

SIR,—In their article (April 23) Dr Phear Dr Sherlock, and Dr Summerskill have shown that the administration of ammonium chloride and methionine to two patients was followed by gross mental deterioration culminating in coma They state (p 838):

> As in case 1 *therapeutic* [my italics] administration of ammonium chloride caused the blood-ammonium level to rise before clinical deterioration took place and again recovery coincided with a fall in the blood-ammonium level. Following oral *dl* methionine a relapse was associated with a rise in the blood-ammonium level

The manner by which this information was obtained raises moral and ethical questions. No doubt the relationship between the level of blood-ammonium in liver disease and the production of mental changes is important to medicine. However, this information had already been obtained by other workers to whom reference was made in their opening paragraph (p 836) In order to prevent a premature or rash judgment on the moral issues involved would Dr Phear and her colleagues be good enough to answer the following queries

(1) Did they know that ammonium chloride and methionine were potentially dangerous to cases 1 and 2 before the drugs were administered? If they did why was it necessary to confirm the knowledge?

(2) Were the patients consulted *before substances* potentially dangerous to them were given and did they agree to participate in the experiments?

(3) If the patients did agree were they capable of fully *understanding* the nature of the therapeutic experiments and the dangers involved? From figs. 4 and 5 it would appear that they were not mentally normal before the noxious substances were administered

(4) If one of the patients had died in coma during the therapeutic trial would the coroner have been informed and given the full story?

(5) Would they have performed similar experiments on themselves or on their near and dear ones supposing they were clinically suitable?

Medical research workers who are concerned with human lives have to steer carefully between the production of fruitful work and the obligations of the Hippocratic oath In this spirit, I look forward to a satisfactory reply

Pathology Department,
Birmingham Accident Hospital　　S SEVITT

*** This letter has been shown to the authors of the article whose reply follows—ED L

We are glad to answer Dr Sevitt s points

1 Ammonium chloride (in the management of ascites) and methionine (on the nutritional hypothesis) are currently used therapeutic agents in the treatment of liver disease. Our paper concerns therapeutic trials *not* experiments Ammonium chloride and methionine were administered to these individual patients in order to diagnose accurately their mental and neurological illness. As we have concluded in this paper there is no certain biochemical method of diagnosis, and transitory mental and neurological deterioration *after* methionine ammonium chloride or a high protein diet are the only certain diagnostic tests we know Simple protein restriction is not a certain diagnostic method for we have observed patients with chronic portal systemic *encephalopathy* who have failed to respond to it. The diagnosis of these complications can be extremely difficult and later experience makes us think we may have over-simplified the issue in our earlier paper (*Lancet* 1954 ii 453) Certain diagnosis can of course be followed by correctly applied treatment *Trials* of this nature in patients with obscure mental and neurological illnesses will prevent many being admitted as certified insane to mental hospitals We have recently known of

six such instances We also give courses of ammonium chloride and methionine to candidates for porta caval anastomosis, where the development of mental or neurological changes contra indicates the operation It is unjustifiable to perform this operation without such a preliminary trial

2 The patients were aware of the nature of the substances they were to receive (they had had them before therapeutically in other hospitals), and that it was necessary for diagnosis to determine their effect They knew that temporary mental and neurological deterioration might follow, and willingly agreed

3 They were capable of understanding the nature of the trial

4 Under conditions of careful observation by the team here (which includes a full time trained psychiatrist alert to the earliest mental changes in liver disease), the possibility of permanent sequelæ or fatal issue due to these drugs is non existent The changes are transient and reversible The coroner would of course always be informed of unexpected death during any treatment

5 If we or our relatives suffered from liver disease and had mental changes or had an obscure organic psychosis or neurological illness it would be necessary, under hospital observation to determine the effect of nitrogenous substances including ammonium chloride and methionine

Dr Sevitt rightly emphasises the moral and ethical issues involved in our efforts to diagnose our patients' ills and in attempting to define more accurately the management best suited to their needs Like other members of our profession we are constantly guided by these moral obligations to patients who have sought our help or have been referred to us as difficult problems It was this moral obligation which prompted us to report our observations in the medical press and thereby draw attention to this complex and ill-understood aspect of liver disease This may provide guidance for others in the diagnosis and management of obscure organic psychoses, prevent unnecessary certification, and possibly prevent the present abuse of a high-protein diet and other nitrogenous substances in the treatment of liver diseases

We will be pleased to meet Dr Sevitt so that we can discuss the matter more fully and perhaps show him the clinical management of patients with liver disease in this hospital

INSTINCT AND THE NURSING COUPLE

SIR,—I would like to congratulate Dr Mavis Gunther on her interesting observations on nipple protractility, in her article of March 19, and to concur entirely when she says that, in human mothers, instinct does not ensure maternal efficiency in breast-feeding

This is perhaps made more obvious by the present day contrast between the high incidence of failure in the West and the almost universal success amongst tropical peasant mothers For example, in Yorubaland in Western Nigeria, of 208 children aged between one month and two years who were investigated, all were found to be still breast feeding successfully[1] Similarly, an as yet incomplete infant feeding survey in rural West Bengal has shown uneventful and continuous breast-feeding in all of over 150 infants aged between one month and thirty months so far investigated—with the exception of a small number where death or very severe illness of the mother made breast feeding absolutely *impossible* In both of these surveys, a high proportion of the nursing mothers were markedly malnourished

As to the factors suggested by Dr Gunther as being responsible for success or failure of breast feeding, I would offer the following comments and additions

(i) *Instinctive response*—This certainly appears to predominate in the infant rather than the mother, but the newborn baby will have more chance of successfully making contact if he is lying on a mat by the mother's side with the breasts near at hand, as occurs with the tropical villager

(ii) *Learning by observation*—From infancy Asian and African peasant females are surrounded by women unconcernedly and unashamedly breast feeding their children, not only in the house, but anywhere and at any time of the day or night

(iii) *Psychological factors*—The Western woman frequently approaches breast feeding not only in ignorance of practical details, but often with some, at least, of the following psychologically disturbing attitudes a fear of failure (engendered to some extent by modern old wives tales), a clear knowledge that easily accessible alternatives are available (which has been drummed into her since childhood by ubiquitous advertising), a desire to return to work or social life as soon as possible, and sometimes a dislike of the whole process or even in extreme cases an alleged disgust All of these can interfere with the mother's confidence and ability, so that, as stressed by Verhœstraete,[2] the disastrous snowball effect of worry—poor "let-down" reflex—dissatisfied baby—increased worry, &c occurs, associated with a diminishing output of milk from inadequate mammary emptying By contrast, the tropical peasant woman (and her Western cousin until quite recently) approaches breast-feeding not with confidence, because this is too positive a word, but a completely matter of fact naturalness Without being conscious of it she knows from personal observation that breast feeding is a simple process carried on uneventfully, while at the same time her attention has not, as yet, been distracted by the advertising of artificial foods In this context, it is interesting to note that, according to Cicely Williams (personal communication) European women, pregnant when interned by the Japanese, were later all able to breast feed their babies when faced with the uncompromising reality of a Singapore internment camp

(iv) *Shape of breasts*—Dr Gunther's investigation of nipple protractility is of great interest As far as I am aware no investigation of breast or nipple shape or size has been carried out amongst tropical peasant women My impression amongst West African women was that, possibly as a result of a lack of any type of support, the breasts were somewhat pendulous even before childbearing Certainly after the first baby the breast becomes flat in the upper half and rounded and pendulous below, presumably partly as a result of uncontested gravity, so that babies can easily be fed per axilla when carried on their mothers' backs In these women the nipple protractility should, one would have thought, have been excellent and have acted as a good "sign stimulus"

It is also interesting to note that the aboriginal Juangs of India divide female breasts into different groups according to their alleged milk giving potentialities[3]—from the *latop nunon*, which is flat like a tortoise and has a poor yield, to the *bagh nunoro* the rounded, so called "tiger breast" which is reputed to have an abundant and easy flow One wonders whether there may be some association in this classification with nipple protractility and ability to act as a "sign *stimulus*"

To close this short picture of the contrast between the over sophisticated Western mother and her counterpart in the tropical village, I cannot do better than quote Matthews's excellent description of the latter as seen in Nigeria

> "Her hormonal mechanism is undisturbed by anxiety complexes She is not besieged by friends, relatives, nurses and doctors advising her against breast feeding and putting her 'at the mercy of the accumulated gossip of her time' She does not receive, within a few days of confinement suggestive pamphlets from infant food manufacturers encouraging early weaning, nor is the Yoruba neurotically prejudiced against the nursing experience as being 'messy' and 'disgusting', nor does modesty prevent her feeding her baby in the markets, by the road side or, if she be a nurse, in the anteroom of the hospital ward What does she care if she lose her figure and her vein marked breasts sag over her umbilicus? Parenthood is her central interest, duty and pride"[4]

Calcutta

D B JELLIFFE

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[1] Jelliffe, D B Malnutrition in African Mothers, Infants and Young Children Report of 2nd Inter African Conference (C C T A) on Malnutrition London 1954 p 230

[2] Verhœstraete, L Epidemiology of Breast feeding (in the press)

[3] Elwin, V Man in India 28 1 Notes on the Juangs 19

[4] Matthews, D S *J trop Med* (in the press)

MEDICAL TELEVISION PROGRAMMES

SIR,—I protest against the programme shown on the B B C television service on May 2 Some elementary physiology was demonstrated with living subjects but the whole presentation was to me revolting At the point where a demonstrator actually burned with a lighted cigarette the forehead of a subject lying on a couch and connected with wires and tubes to recording gear, I switched the set off with the unanimous consent of my family Surely horror comics have nothing on this programme for pseudoscientific sadism

I hope there will be no more of this sort of stuff on television and that doctors will not coöperate in pandering to the crude public taste for medical sensationalism

Birmingham 15 FAUSET WELSH

HARDENED FATS AND LUNG CANCER

SIR —Dr Nyrop's further letter (April 23) erudite though it is should not be allowed to divert your readers from his original and quite unwarranted contention He has sought to show that a deficiency of essential fatty acids may be a factor in the causation of lung cancer and, more especially, that such a deficiency may be induced by the replacement of butter by margarine in the diet

Something may be said for the introduction of new theories of carcinogenesis, in that they may stimulate useful lines of investigation But as regards the essential fatty-acid content of margarine we are dealing with fact not theory The fact is that it has been shown by animal experiment[1] that margarine contains a substantially greater amount of biologically active essential fatty acids than butter Dietary deficiency in these substances whatever its rôle in carcinogenesis is therefore *less* likely to occur when margarine is eaten instead of butter

Queen Elizabeth College
London W.8 JOHN YUDKIN

ELECTROPHORESIS OF PLASMA-PROTEINS

SIR,—In view of Dr J A Owen s letter of April 23 I feel I should point out that results of a rather similar nature have also been observed in these laboratories details of which will shortly be published in the *Journal of Clinical Pathology* There are, however some points upon which I would like to comment

We do not obtain such distinct double β globulin bands as is illustrated by (*a*) in Dr Owen's letter, unless the serum or plasma is fresh and unless the buffer contains borate Dr Owen s result, in the absence of borate appears to be the exception rather than the rule as is evident from the great majority of published illustrations of paper electrophoresis of sera in Veronal buffer

The reason for the occasional exception is not at present clear; we confirm that the slower β globulin component is undoubtedly labile as it disappears after serum has been allowed to stand at room temperature for several hours or even after storing at −20°C for two weeks. Borate appears to exert a stabilising effect in electrophoresis, but in the absence of borate there may be other factors in Dr Owen s experimental condition which also prevent alteration of the labile component. Contrary to Dr Owen our results suggest that the labile component is converted in aged serum to one of higher mobility and merges with the normal faster β-globulin band.

In his second illustration (*b*) there is also shown a double β band, but in this case the slower component is absent and a band appears just ahead of the normal β band We suggest that this faster component is an artefact produced presumably by enzyme action on one of the β globulins since we have obtained similar results only with sera which have been aged at room temperature for long periods

Alterations in the ratio of the concentration of the two β globulin components in fresh serum or plasma may well be significant in some diseases but it is clearly important that no appreciable alteration to the unstable component should occur during electrophoresis One method would appear to be the use of borate, but in borate alone α_1 globulin has a mobility similar to that of albumin This disadvantage has been overcome by employing a mixed borate veronal buffer, which is now being used in these laboratories for routine investigation Full details will be published in the forthcoming paper

Canadian Red Cross Memorial Hospital,
Taplow Maidenhead Berks. R CONSDEN

A MORPHOLOGICAL CRITIQUE OF TEMPORAL LOBECTOMY

SIR,—In his article (April 30) Dr Crome expresses doubts regarding the validity of the biopsy findings reported, among others in a paper by myself in collaboration with Mr Murray Falconer and Mrs Elizabeth Beck.[1]

In this paper we discussed rather fully the difficulties inherent in the interpretation of biopsy material, and we had taken care to reduce the element of ' subjectivity by controlled serial investigations We also admitted to being inevitably handicapped by not knowing whether similar changes are found in the unoperated temporal lobe or in other parts of the brain In our conclusions which were mainly concerned with ætiological problems, we stressed the preliminary nature of our report and the importance of systematic post-mortem studies of clinically and electrophysiologically well investigated cases of temporal lobe epilepsy as ' they are bound to give a more comprehensive and clearer picture of the histological changes than the investigations of isolated biopsy specimens so difficult to interpret could ever provide '

Such post mortem studies on an adequate scale will naturally take some time to mature Dr Crome s otherwise important and interesting material is deficient in this respect since on his own admission no reliable information could be obtained on psychomotor phenomena hallucinations, and auras owing to the severe mental retardation in the majority of his cases.

The histological abnormalities in our material of 18 cases were severe in 11 consisting either of focal lesions (circumscribed tumours and vascular malformations) or of diffuse cortical and white matter sclerosis Partly overlapping with these cases Ammon s horn sclerosis was found in 7 (not 5 as Dr Crome stated) out of 12 cases in which hippocampal tissue was available for study Dr Crome dismisses Ammon's horn sclerosis as a merely secondary phenomenon due to severe grand mal or other types of anoxia. Although we agree with this view (as we have been at pains to point out in our paper) this does not preclude its primary significance in the clinical manifestations of temporal lobe epilepsy Evidence has been accumulating particularly from experimental studies that Ammon s horn and the neighbouring uncus and amygdaloid complex serve general visceral function and have some relation to behaviour particularly emotional behaviour Their pathology in cases of temporal lobe epilepsy requires, therefore our earnest consideration

In only 4 of the 18 cases doubtful and uncertain pathological changes predominated although even in these some positive findings were recorded There is thus in our material considerable variation of the pathological changes both in quality and quantity as we stated in our paper Should these be causally related to the clinical manifestations of temporal lobe epilepsy this relationship would not be a simple one Perhaps we did *not* sufficiently emphasise this complexity in our preliminary communication but it has been given attention in our more recent publication[2] in which we discussed the possible significance of a genetically determined epileptic factor and of an unspecific effect of the operation by removal of not necessarily diseased centres and interruption of neuronal pathways responsible for the seizure In focusing attention on the complexity of the problem Dr Crome s paper has been very helpful.

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[1] Deuel, H J., Greenberg S M., Anisfeld L., Melnick D *J Nutr* 1951 45 535

[1] *J Neurol Psychiat* 1954 17 270

[2] Falconer M. A Hill, D Meyer A., Mitchell W., Pond, D A *Lancet* April 23 1955 p 8 7

The modern concept of temporal-lobe epilepsy was evolved in the late 1940's chiefly on clinical and electro-encephalographic evidence Anterior temporal lobectomy was introduced mainly on these grounds and, whatever the histopathological verdict, it will continue as long as the therapeutic results justify it

Department of Neuropathology,
Institute of Psychiatry
Maudsley Hospital,
London, S E 5 A MEYER

CIVIL SERVICE MEDICAL APPOINTMENTS

SIR,—It was with the gravest disquietude that I read the recent advertisements in *The Lancet* to recruit doctors to posts within the Civil Service

Perhaps the most glaring anomaly in these advertisements is the statement that there are "promotion prospects," this statement appearing with surprising regularity in every post that is offered This would indeed be a welcome change of heart if it were so, but when the Treasury evidence to the Royal Commission in relation to the claims of the Civil Service doctors is studied the statement becomes ludicrous

Perhaps the intending applicant has not yet studied this evidence, which indicates fairly forcibly the poor opinion the Treasury holds of us doctors in the Civil Service, and they are the people who count when the question of numbers and remuneration of higher posts is under consideration

The additional information given to candidates with the application forms is no more informative regarding these "promotion prospects" A small paragraph states quite simply that certain grades exist, but it does not mention what we all know—that all these posts are filled and any promotion is unlikely in the foreseeable future

It appears to me that this should be made known to intending applicants, for the impression given by the advertisements is far removed from the situation as we know it

TOAD BENEATH THE HARROW

A LIVER POISON WITH UNUSUAL PROPERTIES

SIR,—I have read with interest the letter on icterogenin by Professor Rimington in your issue of April 9, and I am sorry that I did not know of his isolation of the lippia poison when I wrote my first letter I am glad to hear that studies of the icterogenic properties of this remarkable substance are already planned May I suggest some points which I feel are of special importance in further studies with icterogenin?

Firstly, it seems to me important to decide whether icterogenin jaundice be a retention jaundice or a lymphogenous jaundice The poison may act in one of two ways (or perhaps in both of them) (1) by paralysing the bile-pigment excretion through the parenchymal liver cells, and (2) by reversing the secretion of these cells from the normal pathway (blood to bile capillaries) to an abnormal pathway (blood to lymph capillaries) [1,2a]

This may be decided experimentally by collecting the liver lymph (or thoracic duct lymph) during icterogenin poisoning and determining the concentration of bile pigment at different times and comparing it with that in the serum If the possibility (1) is correct a prompt direct diazo reaction in the serum (which is found in lippia poisoning) occurs without the bilirubin having passed the liver cells, and if (2) is correct the existence of a secondary secretory mechanism as pathogenesis of lymphogenous jaundice is proved [1,2a]

If (1) is correct our concepts of retention jaundice must be altered Up to the present our knowledge of experimental retention jaundice has been gained exclusively from studies on partial and complete removal of the liver—a technique which is far from ideal because the removal of the liver is followed by important changes in many vital functions and especially because bile pigment production in the stellate cells of Kupffer, which seems to form the bulk of the bile pigment in higher animals,[2b] is abolished

In this respect it is important to remember that the jaundice of acute yellow atrophy of the liver is accompanied by prompt direct diazo reaction [2c] In this condition all parenchymal liver cells must be considered necrotic or at least completely inactive, while the stellate cells of the liver are relatively unimpaired [2d], so the jaundice in acute yellow atrophy seems to come close to a pure retention jaundice, and thus to be very similar to icterogenin jaundice if possibility (1) is correct. As the two conditions have the prompt direct diazo reaction (van den Bergh) in common, (1) cannot be excluded beforehand

If possibility (1) be correct our theory of jaundice must be altered because, according to current concepts, retention jaundice can only become intense after several days [2e], and this cannot be so if lippia jaundice is a pure retention jaundice, because it reaches high intensity in two to three days Perhaps the high bilirubin levels in occlusive and parenchymal jaundice may be explained by retention without regurgitation or other forms of lymphogenous return of bile pigments to the blood.

Secondly, studies in as many species as possible including both laboratory and farm animals and birds, and, if feasible, volunteers, are highly desirable

County Hospital,
Svendborg, Denmark. TORBEN K WITH.

ENURESIS

SIR,—This correspondence and a sentence in your leading article of Feb 19 ("We are not so well equipped to treat enuresis that we can ignore any promising technique") prompts me to write of some conclusions I have formed from twenty years of dealing, in the main successfully, with enuresis in children

Does not the cause of our lack of success lie in the tendency for the specialist to treat enuresis as a phenomenon of the urinary system alone, and for the general practitioner to take the opposite line and tell the mother that the child needs no help and will "grow out of it"?

It is, of course, true, as you state, that in a certain proportion of children the situation arises from specific pathological conditions of the urinary system, but these cases amount to a very small proportion of those suffering from this very common complaint Elaborate urinary investigations, on the other hand, tend directly to increase the child's difficulties in gaining control, and to hinder the achievement of understanding by physician, mother, and child of the part played by delayed bladder control in any individual child

Surely the kernel of the whole problem lies in the power of the body to use its normal functions both to side-track and express emotional strains?

Do we not all remember the frequency of our visits to the W C while waiting for *viva voce* examinations, and have we not noticed how the frequency and timing of micturition in ourselves varies with the weather and the emotional significance of the day's programme?

This ability of the bladder to respond to factors affecting the whole personality is much more marked in children than in adults There is, also, an aspect of urinary performance additional to the emotional factors described by other correspondents, which is peculiar to children

The adult is used to himself and his physical apparatus he has, alas, in most instances, long ceased to "play," and his excreting organs are only of passing interest to him. On the other hand, in children, curiosity, the desire to experiment, the enjoyment of "play," and the urge to acquire knowledge of himself and his functions, and of the mysterious lacks in his small sisters, leads to a concentration of interest on his excreting organ which can be overlaid with other activities during the day, but returns with full force when these vanish in sleep Then, the child who is disturbed in his personality, as described by Dr Symonds (Feb 26) and who has insufficient opportunity and/or ability to "make friends" with the varied aspects of himself, and to gain release from tension in play, will use his urinary function to achieve this end in sleep

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1. With T K *Acta med scand* 1947 128, 25
2. With, T K Biology of Bile Pigments Copenhagen 1954, a, pp 113, 122 b p 61 c, p 201, d, p 63, e, p 121

It is not the bladder or its controlling mechanism but the ole child who needs investigation and help

The difficulty in the treatment of enuresis arises from the paration between pædiatrics and child psychiatry so at the pædiatrician too often sees only the function and e psychiatrist only the personality and such common ro factors as maturation opportunities for play and nsible education of the mother in understanding both des of her child s nature so often do not appear at all

It has been our custom in our treatment at the Institute Child Psychology to provide a ground floor room with cement floor sloping to the outside with illumination from waterproof ship side lantern which is fitted with sinks at fferent heights, water toys of all sorts and pots and jars d hose-pipes. Here clothed in wellingtons and mackintosh child can work out in real water the drives fantasies and periments and—with the aid of the therapist—clarify e puzzles which lurk in his mind and perhaps tip the balance wards expression of all these through his own water reserves night

As Dr Jackson (April 16 p 822) has so wisely pointed ut, rate of maturation varies enormously in different ildren (though surely he is incorrect in putting the lower mit for bladder control at three years ?) and giving up e desire for elementary water play is a function of aturation.

Institute of Child Psychology,
London W 11
MARGARET LOWENFELD

THE DIFFICULT APPENDIX

SIR,—Mr Kerr ends his interesting article of April 9 with the sentence I have regarded McBurney s point as ½ in. below the midpoint of the line joining the umbilicus to the right anterior superior iliac spine.

This implies that there is some choice as to where McBurney's point may be placed This is not true as is shown by the following quotation from McBurney s original paper [1]

> And I believe that in every case the seat of greatest pain *determined by the pressure of one finger* [italics by the author] has been very exactly between an inch and a half and two inches from the anterior spinous process of the ilium on a straight line drawn from that process to the umbilicus. This may appear to be an affectation of accuracy but, so far as my experience goes the observation is correct.

An asterisk after this sentence points to a footnote which reads as follows:

> “Since reading this paper I have carefully observed three other cases. In two the point of pain shown by pressure with one finger was two inches and in the other an inch and seven-eighths from the anterior spine

George Washington University
Medical School Washington D.C.
ALEC HORWITZ

CHRONIC SYSTEMIC LUPUS ERYTHEMATOSUS

SIR,—Your valuable leading article of April 16 prompts me to report 2 cases I have seen recently

A woman of 45 was admitted to hospital in November 1953 with pneumonia. She had had four attacks and a rheumatoid arthritis during the previous six years. She was found to have bilateral basal bronchopneumonia a rheumatoid form of arthritis, enlarged glands in the right axilla and scleroderma of the hands Hb was 48%. The serum albumin/globulin ratio was reversed and L.E. cells were found in the blood smear Pyrexia persisted for weeks despite treatment with antibiotics. There was an immediate remarkable response to corticotrophin. Pyrexia ceased and expectoration of sputum stopped with astonishing rapidity This patient was discharged on 50 mg. of cortisone daily but later the kidneys were involved with albuminuria and uræmia and she died about a year after discharge

A man of 49 was admitted to hospital in June 1954 following five to six weeks of diarrhœa, with blood and mucus in the stools, and painful swelling of both legs Similar attacks of diarrhœa and pain and swelling in the legs had occurred at intervals for the past five years. He had had many attacks of episcleritis in the previous ten years. He had low fever episcleritis in the left eye cellulitis of the left leg and an anal fissure A barium enema showed appearances typical of ulcerative colitis Hb was 75%. Serum proteins were within normal limits. L.E. cells were found in the blood-smear Treatment with corticotrophin was started a month after admission. The pyrexia ceased within a few days and the diarrhœa stopped with astonishing rapidity The anal fissure healed shortly thereafter This man is out and about on 50 mg cortisone daily

These 2 cases represent a chronic form of systemic lupus erythematosus which appears to be commoner than its acute manifestations [1] Both presented without superficial skin lesions or albuminuria The clue to diagnosis in such cases seems to be recognition of the association of recurrent febrile illnesses such as pneumonia pleurisy, pericarditis conjunctivitis colitis &c with involvement of other systems notably the joints and lymph glands. Examination of the blood for L.E cells may be unexpectedly helpful

North Middlesex Hospital
London N 18
D FERRIMAN

CORPORAL PUNISHMENT IN SCHOOL

SIR —The question of corporal punishment in school and the principle underlying it should be decided on the rational ground whether it is favourable or not to the health of children in general As I see it this is a crucial and pressing issue not perhaps especially for doctors but for any society seriously concerned with the health of its children Perhaps therefore you will allow me to make some points on this question

The parent who nags his child to “ concentrate who censures him for incontinence or thrashes him for pilfering is in the same boat with the teacher who cuffs his pupil for not attending to the board or for adding 2 and 3 to make 11 They are behaving exactly like the mechanist philosopher who by tradition has explained learning in terms of the law of use and the pain pleasure principle The former was based on the idea that repeated stimulation of a sensory nerve facilitated a muscle response the latter that pain inhibited and pleasure facilitated a muscle response

In the last half century the *Gestalt* scientists have produced an overwhelming mass of evidence against a mechanistic explanation of natural processes. They have established that the behaviour of living organisms is governed by the laws of organisation and they use the word insightful ” to characterise the behaviour of all conscious organisms. Let anyone reflect whether a child has ever learned to be generous to control his bladder to solve a problem in mathematics to use crayon, brush, or tool through pain or fear or insightless drill In fact all these abilities are functions of the maturation and differentiation of the brain muscle gland organisation and the insight that depends on them.

That physiological processes like the maintenance of the acid base balance and of the constancy of the internal temperature are organised processes justifies Cannon s use of the phrase the wisdom of the body Cannon has further shown that when an animal is affected by *any* painful situation it mobilises its energy for muscle action designed to relieve the stress and restore the animal s balance and unity *Pain is* thus not a deterrent but a positive incitor to action on the part of an organised being like an animal or child It is stress demanding resolution in action.

I consider that sexual tension grows out of ” emotional tension in general and it is therefore easy to understand the two way traffic between sexual and any other kind of emotional tension I have known a child in whom masochistic behaviour had been evoked in infancy flee from punishment in school as from mortal danger and I have seen a hysterical reaction provoked in a teen-age girl at the mere witnessing of the punishment of other children. Any mode of education which uses punishment as a tool establishes a sado masochistic relationship between child and parent on the one hand and pupil and teacher on the other which will colour the child s whole life

But further the unremitting punitive *tensions* in home and in school to which children are subjected in certain areas are in my opinion a decisive *factor in the production of* serious physical illness. If, as I believe resistance is a condition of energy of the child as a whole then punishment will render him susceptible to illness by lowering his resistance

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[1] McBurney C N Y med J 1889 50 676

[1] Tumulty P A J Amer med Ass 1954 156 947

The analysts maintain that the child can "adapt" by using the punitive tensions of authority to build up his super ego and other internal forces of resistance He will then become a "good" person But he will externalise his "unconscious sense of guilt" and many such individuals are always "looking for something to forbid" and cannot even observe the natural behaviour of children without experiencing an inner compulsion to lay hands on them It is not surprising that analysis is confronted with the paradoxical situation of having to restore to broken lives the unity that they possessed in the beginning

Finally, what moral argument is there on behalf of punishment or the "threat of the withdrawal of love" as an instrument of education? As Kenneth Walker says in his *Sex and Society* "It is a betrayal of every spiritual value we profess to hold in reverence, to use love as a bait or a weapon of coercion"

D JACKSON
County Psychiatrist and Director,
Cornwall Child Guidance Service

Perranporth, Cornwall

A VISIT TO KOLTUSHI

SIR,—I found the article by Mr Ruscoe Clarke and Dr Leonard Crome (April 2) most interesting Of interest, too, were the comments of last week of Dr Mungo Douglas in that they represent a distaste for Pavlov's work which is by no means unusual in the British profession

However, one cannot but contrast the meticulous objectivity of the Pavlov school with the doctrinaire disregard of facts shown by Dr Mungo Douglas Instead of criticising the experimental findings, quoted by Mr Clarke and Dr Crome, he asks the rhetorical question "Is it a study likely to provide the kind of future we should all desire ?"

If it can be shown that the great mass of data accumulated by the Pavlov school is all wrong, or if it can be shown that these facts are without relevance to, for example, gastric function, bronchospasm, or, as suggested by Pavlov, schizophrenia, then it is open to Dr Mungo Douglas to prove his case But, in the scientific world at least, generalisations about vital freedom and enslavement cannot be accepted as a substitute for the dispassionate consideration of established facts

Personally I welcome all facts relating to conditioned reflexes since they touch on some very fundamental problems and suggest some interesting possibilities in clinical application

Sheffield C H FOGGITT

PSORIASIS SPONDYLITICA

SIR,—Dr Lydon (April 30) asks us to support the unitarian theory of the pathogenesis of the rheumatic diseases This concept has, however, in the past, proved unhelpful in furthering our understanding of these disorders of connective tissue Moreover, as Professor Kellgren has pointed out,[1] just as no sensible person would seriously suggest that all diseases of the nervous system have a single ætiological factor, so it is equally unlikely in the case of the diseases of the supporting structures It is probable that research into the fundamental cause or causes of the rheumatic diseases will be easier once a greater knowledge of the normal anatomy and physiology of connective tissue and of the various clinicopathological entities which we call the rheumatic diseases has been acquired

As the expression of a useful piece of clinical observation, I, for one welcome the term "psoriasis spondylitica" used by Dr Fletcher and Dr Rose (April 2)

One other point arises from Dr Lydon's letter he is incorrect in regarding the arthritis of Reiter's disease as indistinguishable from rheumatoid arthritis—it differs from it in the joint "pattern" and in its course Reiter's arthritis predominantly affects the joints of the lower limbs, especially the knees and the ankles, it is also much more benign, and seldom leaves any permanent crippling deformities except in the feet

London W 1 J F BUCHAN

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[1] Kellgren J H *Brit med J* 1952, i 1093

NON-PROGRESSIVE BREAST CANCERS

SIR,—Further evidence of the common occurrence of non-progressive, non lethal lesions, in general indistinguishable microscopically from lethal breast cancer, appears to be requisite for a fuller realisation or acceptance of the limitations of treatment Such evidence is obvious, I think, in the data of two series of cases cited previously[1] and other related data In one series, stage 1 (i e, confined to breast) constituted 50%, the 5 year survival-rate in the whole series was over 60%, and in the stage 1 cases it was 85 6% In the other series the respective figures were 16%, 43%, and 81% Consideration of all factors left no reasonable alternative to the deduction that the majority of stage 1 cancers in the first series were non-progressive lesions, and that they accounted, though not necessarily exclusively, for the unusually high 5 year survival rate for the whole series and largely accounted for the high 85 6% rate in the stage 1 cases The near equality of 85 6% and 81%, and the similarity of both with the rates usually obtained in stage-1 cases, point to similarity in the material providing these rates In other words, as the majority of the stage 1 forming 50% in the one series appeared to be non progressive lesions, it seems a reasonable deduction from the similarity of the survival-rates that the majority of stage-1 cancers in most series are similarly non progressive lesions The high proportion of non progressive lesions in the stage-1 cases could then explain, reasonably and consistently, the high survival rates in the latter In contrast to the contention that stage 1 lesions are progressive lethal cancers in an early and curable stage of development, this explanation is fully compatible with the persistence of level trends in age specific mortality in spite of an increase in stage 1 in the treated cases, compatible, too, with the wide variations in reported survival-rates in different series, and with frequencies of stage 1 and of grade 1 as found at different durations.

This does not imply that all the difficulties of differentiation are confined to stage 1 cases The wide difference in survival time even in well advanced cancer, both untreated and treated, reflects wide difference in the degree of malignancy in such cases That difference is not fully revealed even with grading of tumours by microscopy Lewison, in the Halsted Clinic, carefully re-examined sections from the tumours of patients who had survived ten years or more but found nothing on which to prognosticate the long survival[2] Marley et al found approximately the same five and ten year survival rates in cases *clinically stage 1 but pathologically stage 2 (axillary involvement)* as in cases clinically stage 1 but pathologically stage 1 The rates lay between those in *stage 1 and those in stage 2 (clinically and pathologically)*[3] While the near equality of the survival rates in the two groups could be due to chance, it may indicate a degree of distribution of malignancy somewhat representative of such cases as those described An unidentified increase in such *clinically stage 1 but pathologically stage 2* cases in series treated in successive quinquennial periods could thus be a factor in the progressive increase in survival rates in the cases with *axillary involvement as reported* by several clinics

As Smithers et al. have emphasised[4] survival rates are influenced by factors other than diagnosis and differentiation, such as difference in selection of cases after diagnosis, in staging criteria and their application, in detection of lymph-node involvement, in follow up, in calculation of survival rates, &c. However, when, in fifteen series of different time or place and for which the necessary data were available, the 5-year survivals of stage 1 were deducted from the over all 5-year survivals, the net 5 year survival rates then ranged from about 10% to about 30%, with the majority close to 20% They thus approximated to what might be found in untreated lethal cancers. This suggests that the content of non progressive lesions, as stage-1 cancers, is the most potent factor distorting survival rates and suggests also that the varying inclusion of such lesions accounts for most of the difference between survival rates of untreated and treated cases as well as between the rates of treated cases

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[1] *Lancet* 1954, i, 251
[2] *J Amer med Ass* 1953, 153, 905
[3] *Brit med J* 1953 ii, 787
[4] *Brit J Radiol* 1952, suppl no 4

These points are fully consistent with evidence previously reviewed , fully compatible, too with the findings of Murley et al. that all different treatments gave the same survival rates,[5] and also with the findings of Small and Dutton that some patients with treated breast cancer die at normal rates and others die at increased rates that " mortality in cancers is a constant process, little affected by treatment " and that 'it is doubtful if many more persons are cured by radical mastectomy than by other forms of treatment [6] The deductions or suggestions here really go little beyond what is already well recognised and is implicit in all the efforts that are being made to find a sounder basis for prognosis than microscopy provides.

Department of Epidemiology
and Biometrics
School of Hygiene
University of Toronto

N E McKINNON

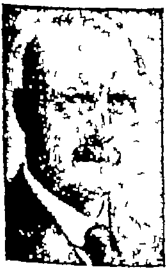
Obituary

HUGH ALLAN MACEWEN

O.B.E. M.B Glasg , D.P H. F R.S.E.

Dr Hugh Macewen a former senior medical officer of the Ministry of Health, died at his home at Innellan, Argyllshire, on April 17

He was a son of Sir William Macewen professor of surgery in Glasgow University He entered the same university and graduated M.B in 1905 He early decided to specialise in public health, taking the D P H of Cambridge and of the London conjoint board in the following year He gained experience as assistant M.O H of Cumberland and M.O H of Fife and Kinross, and later visited the United States, where he was lecturer on hygiene at Cooper Medical College, San Francisco To this period belong his excellent manual on *Food Inspection* his account of *The Public Milk Supply* and his investigations into conveyance of whooping-cough from man to animals by direct experiment


Elliott & Fry

When Macewen was appointed a medical inspector of the Local Government Board Sir Arthur Newsholme then the medical officer of the board lost no time in employing him in important investigations He worked at first in the foods branch and then chiefly directed his attention to epidemiology His *Report on the Prevalence of Poliomyelitis in Certain Districts of Lancashire and Westmorland* (1914) confirmed the views of Wickman Reece, and others that the disease was spread by contact infection

During the first world war Macewen acted as one of the liaison officers between the War Office and the board in the inspection of military camps and hospitals in England and Wales and he was appointed O B E for his services. He became a medical officer of the Ministry of Health in 1919 From then onwards he was chiefly employed in medical administrative work at headquarters. His immediate chief was Colonel R J Reece the epidemiologist, for whom he had a warm friendship Macewen s abilities soon marked him out for promotion and a few years after the establishment of the Ministry he became senior medical officer of the branch of sanitary administration in relation to infectious disease With the passing of the Local Government Act in 1929 the Ministry became concerned with the new municipal hospitals and their efficiency and Macewen was appointed the senior medical officer of the branch which dealt with public health surveys, hospitals, and public-assistance medical services. This work he directed with his usual thoroughness and success. He was in charge of the special investigation into maternal mortality which was published as a white-paper by the Ministry of Health in 1937 In this inquiry his wife, Dr Barbara Cunningham O B E., took an important share. In the early years of the second world war he was in charge of the regional medical organisation, and it was once said that even the evacuation scheme for expectant mothers could not remove the smile from his face

In 1941 Macewen retired from the Ministry but not from medical practice He became medical superintendent of Ballochmyle Hospital in Ayrshire and acted for a time as M.O H of Ulverston rural and urban district in North Lancashire

As a senior medical officer at the Ministry in the 'twenties and thirties he came into close contact with the medical officers of the large local authorities, and as the years went by he came to be more and more trusted by them. Many became his personal friends and one of them, W M F , writes 'Macewen showed his devotion to the cause of public health in everything he undertook. Despite the clinical atmosphere in which he was brought up, as the son of Sir William Macewen, he was convinced of the supreme importance of preventive medicine Before he began his long and successful career at the Local Government Board and at the Ministry of Health he was a medical officer of health and after his retirement, he became—temporarily—a medical officer of health again. To him and his colleagues at the Ministry we owe the rapid development of the personal health and hospital services during the twenty-one years between the first and second world wars. He possessed to an unusual degree the characteristic of selflessness Though he rose to a senior position at the Ministry it was impossible to detect in him any signs of overweening ambition Incapable of jealousy for himself he was jealous of the reputation of the English public health service '

A. S MacN writes Hugh Macewen was a man whose life and work were dominated by high ideals, and his sense of duty and devotion to the public weal never wavered He was serious in disposition except on social occasions when he would unbend and reveal a sense of humour He retained his Scottish accent, was outspoken in his beliefs and while just and considerate to his medical officers, demanded and obtained the best from them Much of his valuable work for the Local Government Board and the Ministry of Health is to be found in official files reports, and blue-books, and in all he did he worthily maintained the high standards and traditions of the central health department "

A colleague at the Ministry of Health writes Around 1930 a number of medical officers entering the Ministry were lucky in having Hugh Macewen for their chief and mentor The formidable exterior soon revealed beneath it a real kindness, a devotion to duty and a passion for accuracy which would never tolerate slapdash work. Verify your references —in the widest sense—might have been his watchword The department lost something of the old traditions and standards of the Local Government Board when he left, though he was able to do excellent work in Scotland both during and after the war He finished a fine life beside his beloved Clyde

HORACE BRYDEN HILL

M.B. Lond M R.C.P

Dr Horace Hill, medical superintendent of Laverstock House Salisbury who died on April 25 at the age of 70 was a man of considerable versatility

After qualifying from St Bartholomew s Hospital in 1901 he held house-appointments at Barts and at Huntingdon County Hospital In 1907 he took the M B Lond., and about this time he joined the Royal Navy and became a member of the staff of the Royal Naval Hospital at Haslar He had always been an all round athlete : an international hockey player and a member of the United Services cricket XI he also took a keen interest in boxing and played water polo This background led to his appointment to the staff of the Naval school for physical training at Portsmouth and later he became instructor in physical training at the Royal Naval College, Osborne In 1911 he took the M R C P

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[6] J Amer med Ass 1955 157 216

During the 1914–18 war he served as a medical officer in H M S *Highflyer* He was made knight in the Order of St John of Jerusalem for his reorganisation of the training and service conditions of the Royal Naval Auxiliary Sick Berth Staff Reserve He also collaborated with Naval officers in an investigation of the best method of applying discipline in the Royal Navy He was made a chevalier of the Order of the Crown of Italy for his work in the Messina earthquake

After the war he left the Navy and settled in practice in Harley Street, joining the staff of the Royal Chest Hospital, City Road He was a vice-president of the Medical Defence Union In 1930 he published a handbook for students on *Electrocardiography* In 1936 he became medical superintendent at Laverstock House His later publications reflected his responsibilities and interests in this new appointment In his brochure in the *Public Attitude towards Mental Disease* (1939) he pointed out how desirable it was that relatives should not delay in seeking early treatment for a patient He also published a useful little book on safeguards in certifying those of unsound mind, and a more formal treatise on *Histamine and Insulin Treatment of Schizophrenia* (1940)

He was no mean painter, and some of his paintings hang in the Royal Fowey Yacht Club where he used to spend much of his leisure His widow survives him

DAVID WINN HOODLESS

O B E , B Sc Lond , L M S S A

WHEN Dr Hoodless was appointed the first principal of the Central Medical School in Fiji in 1929, he was already known, loved, and respected in the Pacific, for he had spent almost twenty years in the Colony as a schoolmaster and later as its director of education

Though his father was an engineer Hoodless came of farming stock He was born in 1887 in a small village in Nottinghamshire, and was educated at Sheffield and at King's College, London, where he gained a gold medal for mathematics, graduating B SC with honours in 1910 His first post as a teacher was in the training ship H M S *Worcester*, where he specialised in mathematics and navigation Two years later he went to Fiji as headmaster of a school for native boys, and later of the Queen Victoria School at Suva Through his work he came into close contact with the Fijian people, and his wish to serve them turned his thoughts to medicine In 1919 he came to England for two years to study at Charing Cross Hospital In 1921 he returned to the Pacific as inspector of schools in Fiji, and the following year he was appointed director of education During the five years that he held this post he established five new provincial schools to serve the Indian as well as the Fijian communities and started a scheme for recruiting teachers from New Zealand Such was his determination that he returned to England in 1928 to continue his medical studies, but illness prevented him from taking his finals in 1929 Despite his lack of formal medical qualifications he was wisely appointed the first principal of the Central Medical School When he qualified in 1935 he also took the diploma of tropical medicine

Hoodless did his task in Fiji so well that he was sent to inspect medical schools in Africa, but when the war broke out in 1939 he was recalled as he was indispensable to the Fijian government On his retirement in 1947 he was appointed O B E He was an associate of King's College In 1953 he became correspondent to *The Times* in Fiji

P M-B writes "The name of Hoodless was one to conjure with in the Pacific He probably did more for medicine and education in Fiji than almost any other man He was the moving force behind the Central Medical School for Polynesians in Suva, and it must have been a great satisfaction to him when two years ago the Queen opened the fine hostel for Polynesians and the ancillary teaching blocks at the school An even greater satisfaction to him was the renown which the graduates of his school won from so many quarters during the late war Many of the Allies, mostly the Americans, were amazed at the knowledge and efficiency shown on many a lonely Pacific atoll by the Polynesian doctors who had been educated in Suva It was the greatest compliment to him that the American government for the island of Guam and the New Guinea government sent their quota of medical students to Suva Throughout the myriad islands of the Pacific he will be mourned as the guide, philosopher, and friend of the Polynesians, for he not only taught but guided and advised them as the ideal leader of their youth "

Dr Hoodless married in 1923 Miss Hilda Adlington, and there is a daughter of the marriage He was on holiday in this country with his wife when he was taken ill in Cambridge He died on April 15

Dr EGBERT MORLAND

S T writes Egbert Morland was a connoisseur of "obits" Not for him the list of dates and appointments culled from the reference books Every obit must stand on its own merits To write dully about the dull was a sin against the craft of journalism The ethic of happy curiosity, which he professed, made him certain that no life could be so barren as to yield nothing of interest and it was the thing of interest alone which was worth recording But a good obit must not only interest, it must entertain, amuse, or edify It must tell the truth without unduly offending the relatives It must please friends and pacify enemies It must follow no logical pattern, but must blend fact and interpretation into a whole, having an artistic integrity of its own And if on reading it, our eyes are filled with that divine mixture of laughter and tears, then it may be said to have succeeded

Egbert's attitude to obits followed from his rational Christian view of death Dying might be very unpleasant but death was a brief moment of transition only and the gateway to another "awfully big adventure" He saw no reason to doubt the spiritual validity of Christ's promise of immortality So when those we know or love come to die, selfish sorrow at our loss should deliberately be replaced by joy at their good fortune For Egbert, the conventional condolences and the trappings of mortality were a source of endless delight and amusement

I think Egbert was a Benthamite, a pragmatic utilitarian, to whom happiness was very important indeed He wanted everybody to be happy, and saw no reason why he should not begin with himself

Despite an occasional witticism at the expense of reformers, he was a reformer himself He was seeking ever to make the world happier, wiser, and more amusing He was not always sure of the precise course to follow, but he turned this multivalence to positive advantage He would back people rather than plans Having picked his men or women, he would test them and try them with every devious tortuosity he could devise If they still came up smiling, or at least came up, he would give them their head At times, indeed, his trust was almost alarming So we of his staff were able to become once again "those sharp *Lancet* fellows" who had fought the good fight a hundred years before

Arrogance as a cloak for ignorance he would not tolerate Indeed the puncture of pomposity was a favourite occupation There was no subject on which he was ashamed to confess that he did not know, and he expected a like humility in others He had no patience with the establishment of a committee as an excuse for inaction, and his gentle ruthlessness was often an unpleasant surprise to the "No" men of his day

It would be incorrect to say that the truth was not in him But sometimes it took a lot of finding "Always remember," he told me, "that in journalism interest is more important than accuracy" He held the view that the only purpose of writing was to be read If this failed then the whole thing became a sterile intellectual exercise For the same reason, he loved the stimulating or provocative headline, the carminative which tempted the lazy appetite into operation The right place for the purely descriptive heading was the abstracting journal

Egbert's insight into his tortuosity was complete "Whether I have continued to edit *The Lancet* or become an inmate of Brixton has rested upon a knife-edge A single tiny genetic alteration and the coin might have come down the other way I hope I am enough of a knave not to be a fool"

As the years rolled by, his obliquities became more oblique and the knight's moves of his mind took on an ever more fanciful pattern "I cannot solve your problems, my dear fellow at best, and even this is improbable, I may perhaps enable you to solve them for yourself" We were talking under a mighty tree in an Aylesbury garden and I left him with none of my conflicts resolved Yet over the months they melted away as perhaps he intended they should. Years before, when I had been tortured by doubts he had joyously put me on the right road when he finally saw he saw with great clarity

Dear Egbert to have worked for you and with you was a joy which time dims not at all To skip and picnic again with you and Mary in the Elysian Fields beyond the Chilterns robs death of its last remaining sting

E M C writes Your obituary notice of Dr Morland gives a vivid picture of his many sidedness I knew him for many years, but he still had a few surprises up his sleeve and of course lots for the unwary who thought him merely eccentric or affected We once had the great joy of a holiday shared with him his wife and family, and several young relatives. Led by him, the younger end of the party set off over the Gross Glockner pass to spend the night in the hut and go on to see the sunrise By then we were well acclimatised to the sun but I had had little experience of summer sun off the snow and by the evening my face was a mess with sunburn Next day after one look at it, Egbert said quietly, You and I are going to walk home by the valley, and leave the young ones to go over the top This was a great disappointment, but I couldn't question his judgment for I knew he was right. What I did not know was what a treat was in store, for his knowledge of Alpines was encyclopædic. I shall never forget that walk, taking it easy and stopping to look at first one and then the next little masterpiece, held out for me to see or just lifted up from the edge of the snow He felt a little guilty not to have warned me about the sun the day before, but, characteristically, it was the plants with which he was tender

Appointments

ANNELS, E. H., M.B. Lpool, D.P.H. deputy county M.O. Flintshire
KOHN JOACHIM, Med Dipl Lwow D.C.P. consultant in pathology Queen Mary's Hospital Roehampton
MOTVAGH, D W, M.C. M.B Lond, D.P.M whole time senior asst. psychiatrist, Mapperley Hospital Nottingham.
RALPH, L. L. M.B Sheff. D.M.R.D part-time consultant radiologist, Chesterfield and Mansfield groups of hospitals
SALFIELD D J, M.D Düsseldorf D.P.M whole time children's psychiatrist, Derbyshire county council

North East Metropolitan Regional Hospital Board:

ARNOTT D C. M.B Lond., D PHYS. MED D.C.H part time consultant physician in physical medicine Queen Mary's Hospital for the East End and St Mary's Hospital Plaistow
FOXELL, A. W. H. M.B Lond consultant pathologist group laboratory, Mile End Hospital
GRUNBERGER, GEORGE M.D Basle D.L.O part time consultant E.N.T surgeon, Queen Mary's Hospital for the East End
FAUL, RICHARD, M.B. Lpool D.M.R.D part time consultant radiologist St. Leonard's Hospital

Appointed Factory Doctors:

HOUGH F G, M.B., N.U.I Tuxford, Nottingham
McCALLUM E. L. R. M.D Toronto Richmond York.
RHYS-DAVIES N C. M.R.C.S Milborne Port Somerset.
WADE O T, M.R.C.S Radcliffe Nottingham.
WILSON A H L. M.B Glasg New Abbey Kirkcudbright

Colonial Appointments:

BUTLER, G C., M.B N.U.I D.P.H: senior M.O sleeping-sickness service northern region Nigeria
CHAMBERS, H D M.B Aberd: senior M.O, Jamaica.
CUMMIR J R., M.R.C.S pathologist, Sierra Leone
FRANKS I I M.R.C.S. L.O.M.S specialist officer (ophthalmologist) Federation of Malaya.
FERN G C., M.B Lond F.R.C.S: M.O (grade II) Trinidad
JONES D J M.B. Wales: M.O., Federation of Nigeria.
RITCHIE, JEAN K., B.M Oxfd M.R.C.P D.M.R.T: radiologist Singapore
SCHURRER, W., M.D M.O Gold Coast
THOMAS M.O L.R.C.P.I: M.O., Sierra Leone

Births, Marriages, and Deaths

DEATHS

ANNAND.—On May 6 at 7 St. Andrew's Road Coventry William Fraser Annand, M.D. Lond., aged 75

Diary of the Week

MAY 15 TO 21

Monday, 16th

UNIVERSITY COLLEGE, Gower Street W C.1
4 45 P.M. Prof E L Smith (Utah) Mode of Action of Proteolytic Enzymes (Second of three lectures)
UNIVERSITY OF ST ANDREWS Queen's College Dundee
5 P.M. Dr R Heim de Balsac (Paris) Vascular Factor in the Radiology of the Lung fields

Tuesday 17th

UNIVERSITY COLLEGE
5 15 P.M Dr J D N Nabarro Adrenal Cortex and Renal Function (Cushny lecture)
ROYAL SOCIETY OF MEDICINE
3 30 P.M (London School of Hygiene and Tropical Medicine Keppel Street W C 1) *Epidemiology and Preventive Medicine* Meeting to celebrate centenary of publication of Snow's work on cholera
4 30 P.M (1 Wimpole Street, W 1) *Proctology* Mr Harold Edwards, Dr E N C McAmmond (Vancouver) Dr Raymond W McNealy (Chicago) Mr Stanley Aylett Diverticulitis of the Colon
WRIGHT-FLEMING INSTITUTE OF MICROBIOLOGY St Mary's Hospital Medical School, Paddington W 2
5 P.M. Mr A T R. Mattick, PH D Lactobacilli and some Streptococci
INSTITUTE OF DERMATOLOGY St. John's Hospital Lisle Street, W C 2
5 30 P.M. Dr S C. Gold Drug Eruptions

Wednesday, 18th

POSTGRADUATE MEDICAL SCHOOL OF LONDON, Ducane Road W 12
2 P.M Prof G Payling Wright General Pathology of Tuberculosis. (Last of three lectures)
ROYAL SOCIETY OF MEDICINE
5.30 P.M *General Practice* Lady Barnett M.R.: T V and the General Public
INSTITUTE OF DERMATOLOGY
5.30 P.M Dr J O Oliver Prevention of Hospital Infection
SOUTH WEST LONDON MEDICAL SOCIETY
8.30 P.M. (Bolingbroke Hospital Wandsworth Common S W 11) Mr A Dickson Wright Varicose Veins, (Bolingbroke lecture)
HYPNOTHERAPY GROUP
8 P.M (1 Wimpole Street, W 1) Dr A Fry, Dr N S. Sherrard Dr R. M. Harrison Dr R B J Ridge Hypnotherapy in General Practice.

Thursday, 19th

ROYAL COLLEGE OF SURGEONS OF ENGLAND Lincoln's Inn Fields W C.2
5 P.M. Mr H R. S Harley Subphrenic Abscess
POSTGRADUATE MEDICAL SCHOOL OF LONDON
4 P.M Dr C M. Fletcher Atmospheric Pollution and Disease
UNIVERSITY COLLEGE
4 45 P.M Professor Smith Mode of Action of Proteolytic Enzymes. (Last of three lectures.)
BRITISH INSTITUTE OF RADIOLOGY 32 Welbeck Street W 1
8.30 P.M Mr J A. C Fleming Position and Scientific Rôle of the Institute (Presidential address)
ROYAL SOCIETY OF TROPICAL MEDICINE AND HYGIENE, 26 Portland Place W 1
7.30 P.M Prof A Corradetti Studies on Comparative Pathology and Immunology in Mammal and Bird Plasmodium Infections
WEST LONDON MEDICO-CHIRURGICAL SOCIETY
8 30 P.M. (Royal College of Physicians Pall Mall East S W 1) Sir Charles Dodds F.R.S Renaissance of Treatment (Cavendish lecture)
HONYMAN GILLESPIE LECTURES
5 P.M (University New Buildings Teviot Place Edinburgh 8) Dr J H Wright: Unilateral Renal Hypertension
UNIVERSITY OF ST ANDREWS, Medical School Small's Wynd Dundee
5 P.M Prof Alan Kekwick Obesity

Friday, 20th

UNIVERSITY OF LONDON
5 P.M (St Thomas's Hospital Medical School S.E.1) Prof V Erspamer (Bari) Biological Significance of 5 hydroxytryptamine and Related Substances
POSTGRADUATE MEDICAL SCHOOL OF LONDON
2 P.M Mr A I. d Abreu Surgery of Congenital Heart-disease
4 P.M Dr Ian Douglas Wilson Words without End
UNIVERSITY COLLEGE
5 15 P.M Dr Harry Harris: Genetic Aspects of Tubular Function (Cushny lecture)
ST MARY'S HOSPITAL MEDICAL SCHOOL, W 2
5 P.M Dr I. B W Brimblecombe: Lactation and Breast-feeding
FACULTY OF RADIOLOGISTS 45 Lincoln's Inn Fields W C 2
4 30 P.M Dr S Whately Davidson Anomalies of the Respiratory System (Skinner lecture)
OSLER CLUB
8 P.M. (Royal Army Medical College Millbank, S W 1) Sir Gordon Gordon Taylor Reminiscences of Some Famous Surgeons of the 1914–18 War
UNIVERSITY OF ST ANDREWS Queen's College, Dundee
2.30 P.M Dr J H Wright Dr R. W D Turner Prof Robert Walmsley Dr K. G Lowe: Pulmonary Stenosis as an Isolated Lesion and with associated Atrial Septal Defect (Fallot's trilogy)

Notes and News

HEALTH CENTRES AT YORK AND STRANRAER

WITHIN the past month two new health centres have been opened—at York and Stranraer

Performing the ceremony at York on April 14, Sir John Charles, chief medical officer of the Ministry of Health, declared that there was nothing so inspiring, so apt to promote smooth and efficient performance, as the outward and visible signs of bricks and mortar—such a sign as the new centre The centre is in the middle of a large post war housing estate and it will serve a population of about 25,000 In the first place, it will provide maternity and child welfare, health visiting, school nursing, and dental services, but the building has been designed in such a way that an extra wing of consulting rooms for general practitioners can readily be added later Alternatively, general practitioners may rent some of the existing accommodation, and discussions on this question are in hand The centre has been planned so that different kinds of patients are in independent units but they can all be easily supervised from the central administration offices The cost of the present building was £13,000

Stranraer's health centre is the second to be newly built in Scotland (the other is at Sighthill in Edinburgh [1]), and the first to be built adjoining or connected to an existing hospital It contains five consulting suites for the general practitioners of Stranraer, who have a total of 13,200 people on their N.H S lists In another wing there are three rooms and a dental workshop for local authority services, and the local authority will share another four rooms with the board of management responsible for the adjoining Garrick Hospital In addition the hospital has for its own use a changing room, a plaster room, and rooms for an X-ray unit The cost was about £33,000, of which the hospital authority will contribute some £12,000 The centre was opened on May 6 by Mr H R Smith, secretary of the Department of Health for Scotland

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University of Oxford

On April 28 the following degrees were conferred

D M—Zelda M Hall Constance L Simpson
D Sc—W Ritchie Russell

University of Glasgow

On April 30 the following degrees were conferred

M D—M C Macleod (honours), R C MacLeod.
Ph D—T C D Whiteside

Royal College of Physicians of Edinburgh

At a meeting of the College held on May 3, with Sir Stanley Davidson, the president, in the chair, the following were elected to the membership

J M Johnston H R. Harris T M Desai L Molk M. B Azami R H Aldons S K Mazumdar, D O Lewis, D A Kerfoot E N A Magid, J Richmond, E Schiller W G Smith S S Levin E S Nash J R. Shah B C Syam I J Pinto R C Parikh N H Brooke S C Jain, B Cowan, R. H C Rischbieth W H Wolfenden J C Pond M Wakefield, G D Campbell, B C Paton, M A Kibel

Hunterian Society

Mr A Dickson Wright has been elected president of this society for 1955–56

Royal Society of Tropical Medicine and Hygiene

The Chalmers medal for 1955 has been awarded to Dr W E Kershaw, lecturer in medical parasitology, Liverpool School of Tropical Medicine

N A P T Travelling Fellowship

The Scottish branch of the National Association for the Prevention of Tuberculosis offers a travelling fellowship (£250), for postgraduate study abroad, to a doctor working in Scotland on tuberculosis Applications should be sent not later than July 15 to the Scottish secretary, N A P T, 65, Castle Street, Edinburgh, 2

British Society for Research in Ageing

This society will hold a symposium on Thursday, June 9, at 2 P.M, at 41, Portland Place, London, W 1, on Endocrinology and Ageing Prof G R Cameron, F R S, will be in the chair The speakers will include V Korenchevsky (London), J A Loraine (Edinburgh), P L Krohn (Birmingham), and P J Thung, L Boot, and O Mühlbock (Amsterdam) Further information may be had from the hon secretary, Mr G H. Bourne D.SC, London Hospital Medical College, Turner Street, E 1

Sydney Body Medal

This medal has been awarded to Dr L Gordon Hopkins "for his unsurpassed services to medicine during fifty years in Southend."

Medical Records Exhibition

This exhibition will be held at the Bonnington Hotel, Southampton Row, London, W C 1, from 10 A.M to 6 P.M. on Saturday, May 21 At 11 A M Dr N M Goodman will give a lecture on Statistics and Records of Cancer The exhibition has been organised by the Association of Medical Records Officers to help hospital staffs to deal with problems of indexing, correspondence, outpatient waiting, admission and discharge procedure, and storage of records

International Society for Human and Animal Mycology

Last year, at the 8th International Congress of Botany, this society was founded to bring together those interested in the study of fungi living on humans and animals. The president is P Redaelli (Milan) and one of the vice-presidents is G T Ainsworth (Exeter) Further particulars may be had from Prof R Vanbreuseghem, Institute of Tropical Medicine, 155, rue Nationale, Antwerp, Belgium.

Hospital for Tuberculosis in Malaya

Dr M R J Snelling, chest physician at the King Edward VII Sanatorium, Midhurst, has been appointed the first medical superintendent to the Lady Templer Hospital for Tuberculosis at Kuala Lumpur This new hospital, which has 250 beds, is to be run on similar lines to those of the King Edward VII Sanatorium. A thoracic surgeon and a team are shortly to join Dr Snelling, and Australia is sending 28 nursing sisters

French Prize for Medical Film

At the fourth distribution by the *Presse Médicale* of prizes for medical films the prize for the best foreign entry was awarded to C E Engel (London) for his film on *Mitral valvulotomy for mitral stenosis* Honourable mention was given to the film by P Hansell (London) on *Grafting on the cornea* Applications for next year's competition will be received up to the end of next February, addressed to the *Presse Médicale* 120 Boulevard Saint Germain, Paris VI

Nursing Times

The golden jubilee of the *Nursing Times* was marked by a luncheon in London on May 6, under the chairmanship of Mr Daniel Macmillan Sir Harold Boldero recalled that only in the past half-century had nursing become fully established as a profession landmarks in this period included the foundation of the College of Nursing in 1916, the Registration Act of 1919, and the adoption by the college of the *Nursing Times* as its official journal in 1926 He went on to refer with regret to the fragmentation of medicine, and wondered whether the same sort of thing was happening in nursing Did those engaged in teaching nursing—who seemed to spend all their time on this task—go into the wards and see what was being done there? Did district nurses go into the hospitals? The medical curriculum was admittedly overloaded, and he asked whether the nursing curriculum was similarly overloaded or (which came to the same thing) there was insufficient time in which to teach everything included in the curriculum. Miss M. L Wenger, editor of the *Nursing Times*, spoke of some of that journal's activities Recently these had included the encouragement of recruitment to the mental hospitals and the offer of a bursary to enable a nurse to spend a year in the study of journalism, for they believed that nurses should be able to describe the results of their work. Dame Enid Russell Smith enunciated five aims for a professional journal First, it should advance professional knowledge (of course in language understandable to no layman) secondly, it should present professional political issues without bias, bitterness, or personalities, thirdly, it should put the work and aims of the profession in the setting of the fuller scheme of things (the margin between proper professional pride and arrogance was narrow), fourthly, it should set a high standard of professional ethics and support the best traditions (thus acting as the profession's memory); and fifthly, it should encourage the pioneering spirit, so that no reader, after studying any issue of the journal, could feel any self satisfaction at all The *Nursing Times* had succeeded in each of these aims Finally Miss S C Bovill spoke with pleasure of the association between the Royal College of Nursing, of which she is president, and the *Nursing Times*

A draft British standard for gas-cylinder trolleys has been issued by the British Standards Institution Comments should be sent to the institution 2, Park Street London W 1, before June 7

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[1] See *Lancet* 1953 i, 1038

THE CLINICIAN AND
E PROBLEM OF MULTIPLE SCLEROSIS*

Douglas McAlpine
M.D Glasg F R C P
SICIAN IN CHARGE OF DEPARTMENT FOR NERVOUS DISEASES,
DLESEX HOSPITAL, LONDON PHYSICIAN MAIDA VALE
HOSPITAL FOR NERVOUS DISEASES

DURING the past quarter of a century there has been a able revival of interest in multiple or disseminated rosis particularly in America In the laboratory the perimental pathologist has evolved a technique by ich an encephalomyelitis can be produced in animals luding the monkey by means of subcutaneous or ramuscular injections of brain tissue along with an juvant consisting of heat killed tubercle bacilli. The ults of these experiments have suggested to some servers that brain tissue may contain a chemical agent ich acts as an antigen producing antibodies that react h constituents of white matter The part played by adjuvant used in these experiments is uncertain

Meanwhile, clinicians have contributed mainly in two ctions—first in geographical and racial studies and ondly in attempts to determine more accurately the ure of the disease.

Geographical surveys were undertaken first in Switzer d by Bing and Reese (1926) and subsequently in nmark (Gram 1934) Sweden (Sällström 1942), and ts of the United States of America (Kurland 1952) st of these surveys have suffered from one serious fect—namely that the results have been based either death certificates or on information obtained from neral practitioners. Notable exceptions have been those ently carried out by Allison and Millar (1954) in rthern Ireland and by Dr John Sutherland in Northern tland

Allison and Millar personally examined all cases ported to them by general practitioners over a three ar period After discarding 187 cases 700 remained in ich they were satisfied that the diagnosis was either obable or possible Using the census figures of 1951 ey were able to arrive at a prevalence rate of 7 9 per 000 after excluding persons under the age of 20 By termining the geographical distribution by place of set, Allison and Millar found that the disease in rthern Ireland does not affect rural populations more an urban nor did they find any evidence to suggest a cal incidence

Dr Sutherland has recently completed a survey of the ease in the Orkney and Shetland Isles the Western les, and the mainland counties of Caithness Sutherland ss and Cromarty Inverness, and Nairn I am grateful him for permission to refer to certain of his findings questionnaire was sent to all general practitioners in se regions asking for the names and addresses of all pected cases of multiple sclerosis ; replies were received m 93% of practitioners 180 cases were notified of hich 16 were rejected 10 other patients had either ed after the case had been notified or had removed from e region these 10 cases were discarded Of the maining cases 127 were classified as probable and as 'possible cases of multiple sclerosis On the sis of the 1951 census figures Dr Sutherland found an ter-all prevalence rate of 5 5 per 10 000 ; if possible ses were included the figure rose to 6 7 In the Shetland les the relative figures were 11 3 and 12 9 per 10 000 e highest rate yet recorded in Great Britain

In the Northern Ireland and Northern Scotland rveys a significant familial incidence was found to hich I shall refer later

The results of these surveys justify the hope that similar field studies of multiple sclerosis in Great Britain will be encouraged, particularly in areas with a reputedly high prevalence rate

Other contributions made by clinicians in recent years include studies of the course of the disease and its prognosis In the past estimates of its duration were usually based on fatal cases. A notable exception was Byrom Bramwell's (1917) follow up of a series of cases over a period of twenty years However, the main credit for introducing some order into this subject must go to Ragnar Muller (1949) whose conclusions are of particular value because of the size of his material and his application of the statistical method His results and those of other workers including Allison (1950) have shown that the outlook for the patient with multiple sclerosis is considerably better than was formerly supposed

These outstanding contributions must not blind us to the fact that other aspects of the natural history of the disease as well as its symptomatology have been largely neglected in recent years My primary purpose here is to indicate the further value of these two lines of study

Aspects of the Natural History

The Familial Incidence

Preoccupation with the hereditary forms of cerebellar and paraplegic disorder may be the main reason for the long delay in the recognition of a small but significant familial incidence in this disease It was the appearance of Curtius s paper in 1933 that stimulated interest in this subject. He found a familial incidence in 9 4% of 106 cases observed in Bonn and Heidelberg (Curtius 1933 Curtius and Speer 1937) Since no case of multiple sclerosis was detected in a control population he concluded that the incidence of secondary cases in the families of multiple sclerosis patients was considerably raised when compared with a control population Since 8 positive family histories were obtained in a series of 142 cases reported from the Middlesex Hospital in 1946 an additional series was investigated with Pratt and Compston (1951) In a total of 310 cases the familial incidence was 6·5% In the Northern Ireland survey the figure was 6 58% Millar and Allison were the first to compare the expected risk in siblings of patients with multiple sclerosis with the rate in a control population studied in the same area and at the same time They estimated the risk to be about ten times greater in siblings of patients than in the control population and agreed with our view that the excess risk is not due to a common environment or to infection but to a genetically determined predisposition In the Northern Scotland survey there were 12 families with more than one case of multiple sclerosis an incidence of 9·4% This figure errs on the conservative side since in 12 other families there was a positive history but as the diagnosis could not be satisfactorily established in the secondary cases they were excluded Dr Sutherland rejected a diagnosis of multiple sclerosis in three brothers living in the Island of Lewis affected by a progressive spastic paraplegia preferring to regard it as a purely hereditary condition In the Orkney and Shetland Isles the familial incidence exceeded 10% Parental consanguinity seemed a possible explanation for this high figure but the incidence proved to be comparatively low Dr Sutherland's observations which cover racial dietetic and other factors may throw further light on the relative parts played by heredity and environment in this disease

Precipitating and Aggravating Factors

At the end of the last century and the beginning of the present one there are many references in the literature especially German to the effect of such factors as infection injury physical exertion exposure to damp and cold emotional upset, and prolonged worry in unmasking the first symptoms of the disease In 1934 Hoesslin published a monograph devoted to these so called exogenous factors

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*The Florence Tong lecture delivered before the Association of British Neurologists at Cambridge on March 25 1955

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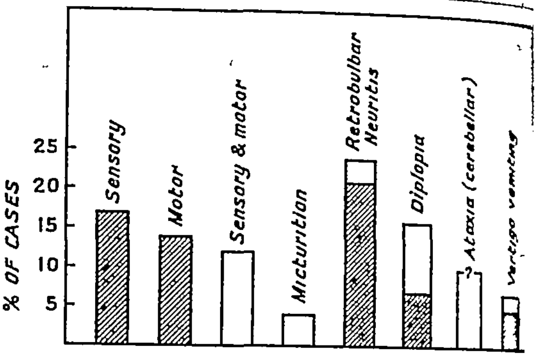
The criteria necessary to establish a causal relationship between a supposed precipitating factor and the onset of the first symptom of multiple sclerosis or a relapse are (1) a temporal relationship, and (2) a significant incidence of the factor in comparison with a control series The time interval is difficult to fix, and a period of three months which we arbitrarily chose in studying these factors seemed reasonable (McAlpine and Compston 1952) However, if it could be shown that a causal relationship may exist between trauma, for example, and the onset of the disease, it would be necessary to visualise a longer time-interval than three months Turning to the second point, the evidence in the literature is of little value judged by present day statistical standards Bearing this fact in mind I propose to discuss briefly four conditions which appear with sufficient frequency in the immediate past history of these patients as to warrant attention

General health —It is by no means exceptional to find that for days or weeks before the appearance of the first symptoms, or accompanying them, the patient has not felt in his or her usual health, has lacked energy, has tired easily, and in addition may have noticed headache and vague pains in the back or limbs On inquiry these somewhat indefinite symptoms may have coincided with a period of overwork or overstrain, but in other patients no adequate cause can be found Although by no means the rule, these premonitory symptoms deserve further study, since if we understood their meaning they might provide a partial clue to the ætiology of the disease

Infection —This usually takes the form of a cold, a sore throat, or influenza Bramwell obtained the high figure of 14% of infections preceding the onset in 200 cases, and Hoesslin 10 5% in 109 acute cases, which is approximately the figure obtained by Compston and myself in 250 consecutive cases Taking these figures and those in other series into account, it may be said that 10% represents the approximate incidence of some form of infection before the onset If attention be paid to this question it will be found that not infrequently in an established case of the disease, a relapse may immediately follow an upper respiratory infection

Trauma —The third factor is trauma, whose occasional relationship to the onset of multiple sclerosis has been commented upon by numerous writers (McAlpine and Compston 1952) In our own series of 250 consecutive cases particular care was taken to exclude trauma from a fall due to the disease In the three months preceding the onset there was a history of trauma, including dental extractions but not surgical operations, in 36 patients (14%) as compared with a similar history in 13 patients (5 2%) in a control series of hospital inpatients With regard to the site and degree of trauma, it has been assumed by most writers that the injury must be cranial or spinal and severe in degree (Keschner 1950) Whether the changes set up in the nervous system are primarily vascular or chemical, there seems no reason to exclude the limbs when considering the site of trauma Hoesslin was the first to suggest that there may be a relationship between the site of the trauma and that of the first symptom Of our series of 250 cases, in 22 out of 36 (61%) patients who gave a history of trauma, there appeared to be a correlation between the site of the injury and the part of the body, usually a limb, in which the first symptom appeared We also showed that the relapse rate within the three months following trauma, whether this was accidental or surgical, was significantly greater than the expected relapse-rate during the same period This evidence, of which fuller details are given in our paper, suggests that slight or severe trauma, including an operative procedure, to a limb or any part of the body, may occasionally precipitate the disease or may be t cause of a relapse



Initial symptoms of multiple sclerosis, occuring alone (hatd columns) or in combination, in 309 cases.

Allergic disorders —The incidence of allergic disord in the past history of patients will naturally dep on the scope of the inquiry In our series we fou no significant difference in the remote past history multiple sclerosis patients as compared with a cont group , but in the three months preceding the onset the disease, and in the subsequent months or years, a a history was obtained in approximately 9%, as com pared with an average of 2 8% in a control series.

If mental stress be added to the factors which I ha mentioned—namely, a lowered state of general heal trauma, infection, and an accompanying allergic disord —it may be estimated that one at least of these occu in a close time relationship to the onset in roughly eve other patient, an estimate which probably errs on th conservative side

Features of the Early Symptomatology

There is still no consensus of opinion as to the relati incidence of the initial symptoms It therefore seems worth analysing the notes of the 309 cases finally dia nosed as multiple sclerosis after admission to the Depar ment for Nervous Diseases, the Middlesex Hospital, und myself and my colleague Dr Michael Kremer, over five year period from January, 1950, to December, 195 Doubtful cases were excluded By limiting the analys to inpatients admitted to the same department it wa hoped that some degree of uniformity in history takin methods of investigation, and final diagnosis would b achieved

In constructing the accompanying figure, motor a sensory symptoms associated with brain stem signs ha been omitted , so the columns marked " motor " a " sensory " refer to cases in which there was a hi probability of one or more plaques in the spinal co Symptoms rarely met with at the onset, such as a isolated facial palsy, have also been excluded

This analysis emphasises the frequency of a mono symptomatic type of onset, which was seen in near two thirds of the cases in this series An isolated retr bulbar neuritis may be expected as the first sign in ab one patient in every five , paræsthesiæ in one out o every six , and thereafter, in diminishing order o frequency, motor weakness (usually in a lower lim double vision, vertigo, and vomiting

One of the characteristic and at the same time puzzl features of multiple sclerosis is the extreme variabil in the mode of onset and duration of the first symptom At one end of the scale is the so-called apoplectifor onset recognised by Charcot , at the other end is the sl insidious appearance of a paraplegia due to spinal plaques How to explain these two modes of onset on the bas of a common pathological process is one of the ma unanswered questions relating to this disease Tr oints, however, should be borne in mind: first the age ncidence differs, an abrupt onset being more common in ounger patients while the slowly progressive form of he disease mainly occurs in those over the age of 40, nd, secondly as in certain other diseases—notably heumatoid arthritis—the individual's reaction to the orbid process can apparently determine the tempo of he initial symptoms and the subsequent course

ransitory Episodes and Exacerbations

The adjectives "transitory" fleeting or short-ved" are often used by writers in describing early ymptoms. The vagueness of these terms leaves the verage reader in some doubt as to their meaning hough he may gain an impression that they indicate a eriod of one or more days. Accordingly serious attention s seldom given to attacks of blurred vision double vision iddiness, or pins and needles in a limb lasting a few ours or even minutes. Yet such episodes are not ncommon in the past history of patients presenting ith undoubted signs of the disease

The factors determining the onset of these fleeting arly symptoms deserve further study So far as my own mited observations go, it seems that, in the main they re similar to those that may provoke more lasting ymptoms I have been struck by the fact that a patient resenting with well marked sensory disturbance in a and, may for several weeks previously have noticed emporary tingling and perhaps numbness in the fingers f the same hand on awaking from sleep or sometimes fter using the hand Likewise an attack of retrobulbar euritis may be preceded by episodes of blurred vision rought on by exertion or emotion The following case s illustrative

Mrs. A aged 23 a hairdresser when playing tennis one ay in September 1953 noticed hazy vision with difficulty in eeing the ball She stopped playing and after a short rest er vision became normal. Subsequently whenever she layed tennis or danced vision was temporarily blurred. In lay 1954, she began cycling to work a distance of about a ile By the time she arrived vision was so poor that she was nable to start work until she had rested for a short time oon afterwards she also noticed numbness in the right hand or some hours after cutting several customers hair in ccession.

In June 1954, vision was 6/5 both eyes, the fundi were ormal and no scotoma could be demonstrated (Mr A J B oldsmith) By July she found that even mild exertion, such s walking quickly affected her eyes to an increasing extent nd soon vision became permanently blurred By October ision was 6/60 in both eyes both discs were pale and a small ilateral central scotoma was now present

On admission in December vision had not improved and he now showed nystagmus and bilateral extensor plantar esponses. After cycling on a fixed bicycle vision became worse comparison of the scotoma in the right eye on an Amsler's hart before this exercise and after four minutes showed that t had markedly extended Five minutes later the central efect had returned to its previous size

To be distinguished, at least clinically from these ransitory initial episodes are the temporary exacerba tions of symptoms which may be a sequel to an estab lished plaque. Of 250 cases investigated by Compston nd myself 82 (32%) gave a history of temporary worsening of symptoms during stress, a finding confirmed y Pratt (1951) An emotional upset may act rapidly n motor function, paræsthesiæ and vision Likewise xertion may have the same effect. These temporary hanges are of course seen in other organic conditions of he nervous system such as traumatic paraplegia but t is our impression that they occur more easily and are nduced by a larger range of exciting factors in multiple sclerosis than in other organic conditions

Franklin and Brickner (1947) suggested that these hanges are due to vasospasm for they observed local ised constriction of retinal arteries during episodes of blurred vision An increased vulnerability of the axis cylinder to chemical influences offers an alternative explanation

Symptom and Lesion

At first glance any attempt to correlate disturbance of function and of structure in multiple sclerosis may seem profitless However not infrequently the earliest symp toms are caused by a focal disturbance, thus permitting a clinical study of their mode of evolution I have in mind particularly sensory symptoms due to invasion of the spinal cord As Oppenheim (1911) originally pointed out tingling and numbness are usually caused by one or more plaques in the posterior columns Furthermore since the cervical cord is often attacked early in the disease a special opportunity is afforded the clinician of studying sensory symptoms, since at that level afferent impulses from all four limbs and the trunk are represented in a known anatomical relationship to each other within a small area (McAlpine 1954)

Although tingling and numbness may be confined to a small area on a limb or the trunk not uncommonly they tend to spread by noting the original site of the paræsthesiæ and direction of spread it becomes evident that this is often determined by the anatomical arrange ment of the proprioceptive fibres within the posterior columns. For example a spread of numbness from a hand to the shoulder and then down the homolateral trunk and finally to the lower limb is indicative of a focus in the column of Burdach extending inwards to the column of Goll. Similarly a spread may take place in the reverse direction Thus the mode of spread appears to be determined by contiguity of structure

Another feature which can be recognised clinically is the symmetry sometimes shown by plaques. For example, it is not uncommon for paræsthesiæ to affect simultane ously or in quick succession corresponding parts of the lower or upper limbs, and be followed by a similar mode of spread in the four limbs A further example of sym metry is provided by retrobulbar neuritis which, contrary to many statements may affect both eyes simultaneously in multiple sclerosis. This symmetrical tendency of plaques, which many years ago was commented on by pathologists poses yet another question for which at present there is no satisfactory answer

Multiple Sclerosis or Spondylosis

So far I have considered certain features of the relapsing and remitting form of the disease Presenting a striking contrast in its mode of onset and its course is the so-called progressive paraplegic or spinal form of multiple sclerosis which chiefly affects the middle-aged

In the analysis of the 309 cases already referred to I came across 27 with signs of a spastic paraplegia in which the diagnosis of multiple sclerosis was at first in doubt During the same period 31 cases of spinal cord compres sion due to tumour (excluding secondary deposits) came under the care of Miss Diana Beck Dr M Kremer or myself. In recent years myelography has substantially reduced the number of cases of cord compression mistaken for the spinal form of multiple sclerosis Today the neurologist, while constantly aware of this pitfall, must also take into account the possibility of cervical spondy losis when confronted with a paraplegia in middle age Over the five year period already referred to there were 30 such cases. An analysis of this group and that of the 27 patients with the spinal form of multiple sclerosis showed that, while the clinical picture in the two groups was broadly similar there were certain points of differ ence First the average age of onset differed in the multiple sclerosis group it was 42 and in the cervical spondylosis group 51, the youngest patient being 27 and the oldest 68 It is in the fifth decade of life however that the distinction between these two causes of para plegia may be difficult A gradual onset and slow progression of motor weakness—first in one lower limb and then in the homolateral upper limb—without any sensory symptoms or signs, may occasionally occur in the progressive form of multiple sclerosis, none of our cases of myelopathy associated with cervical spondylosis showed this pseudohemiplegic type of progression. In multiple sclerosis short attacks of tingling and numbness, usually brought on by exertion, may antedate motor weakness by weeks or months, but such a history is rarely obtained in cervical spondylosis. The spread of paræsthesiæ, when it occurs in multiple sclerosis, tends to be much more rapid than in spondylosis. Pain in the upper or lower limbs is a well recognised feature of the early phase of spondylosis, yet it was not a rare symptom in this small group of multiple sclerosis patients, being among the presenting symptoms in 8 of the 27 cases; it was usually referred to one or both lower limbs or the back. Scattered references to pain in this disease can be found in the literature, and since its interpretation remains in doubt it is worthy of further study.

A history of early disturbance of sphincter control was found more commonly in multiple sclerosis as compared with the myelopathy of spondylosis, the figures being 14 of the 27 multiple sclerosis cases compared with 8 of the 30 spondylosis patients. An episode of temporary incontinence early in the history should suggest multiple sclerosis.

The course of the spinal form of multiple sclerosis is sometimes interrupted by a superimposed relapse; this occurred in 3 cases in this series in the form of paræsthesiæ which developed over the course of a few days and then receded. I have not met with similar episodes in the myelopathy of spondylosis.

Regarding signs, the upper limb reflexes afford little help in differentiating between these two groups of patients—particularly depression or absence of one or more of these reflexes, since this occurred with almost equal frequency in the two groups. While muscular wasting in the upper limb was relatively more common in the spondylosis group, 2 cases of tetraplegia due to multiple sclerosis showed wasting of the intrinsic muscles of the hands, a finding which was commented upon by Déjerine (1884) when he drew attention to the similarity between this form of the disease and amyotrophic lateral sclerosis.

The presence of nystagmus proved to be the most helpful single diagnostic sign; it was present in 14 of the multiple sclerosis cases, but in only 4 of those with spondylosis. In these 4 patients it was purely horizontal in type and was associated with evidence of involvement of the upper cervical cord as judged by exaggeration of some of the upper limb reflexes or by radiological evidence of spondylosis as high as C3–4. In the multiple sclerosis group a well marked rotatory or monocular nystagmus was not unusual and provided evidence of an extraspinal lesion.

Apart from nystagmus, evidence of one or more lesions above the level of the spinal cord was found in 9 of the multiple sclerosis cases; unilateral temporal pallor of the discs (4 cases), mild dysarthria (3 cases), and an exaggerated jaw-jerk (2 cases). Euphoria was noted in 2 patients but only in the course of a follow-up when symptoms had been present for several years.

The findings in the cerebrospinal fluid proved of the utmost value, particularly in those cases in which signs were confined to the spinal cord. 12 of the 27 multiple-sclerosis patients showed a marked paretic curve; in 6 others there was a mid-zone curve of at least 2's. In 1 case the only abnormality was a rise in the protein figure; in the remaining 8 cases the fluid was normal on one or more occasions. By contrast, a mid-zone curve of 2's was only found in 2 cases of cervical spondylosis; in the remaining 28 cases the Lange curve was normal.

Before leaving these two groups of patients, I wish briefly to refer to 8 cases in the multiple sclerosis group which showed clear evidence of cervical spondylosis. The youngest patient was 31 at the onset of symptoms and the oldest 51, with an average age of 42. The diagnosis of multiple sclerosis in these patients with cervical spondylosis was based on the points already mentioned, with the addition of myelography in two cases. In 2 cases protein figures of 130 and 120 mg. per 100 ml. were found.

A woman, aged 44, had for two years received treatment for pain in the neck and left arm due to well marked cervical spondylosis. Rather abruptly she began to stagger when walking and she was admitted under the care of my colleague, Dr. Kremer. Among the positive signs were a pronounced monocular nystagmus, limb ataxia, a mild paraparesis, and a strongly paretic gold curve. She responded only slightly to traction and some months later was readmitted with an abrupt progression of symptoms.

The second case was a male, with onset of symptoms at the age of 31, who five years later was dysarthric and showed temporal pallor of one disc and nystagmus. There was no evidence of block on flexion and extension of the head during lumbar puncture.

It is probable that in these two patients the spondylosis accounted in some degree for the high protein figure. A marked rise in protein occurs rarely in uncomplicated cases of multiple sclerosis. For example, only 5 out of 512 spinal fluids from cases of multiple sclerosis examined by the Courtauld Institute at the Middlesex Hospital showed a figure of 100 mg., or more, per 100 ml.

Conclusions

Certain of the facts mentioned in this lecture may be summarised as follows.

First, of the chronic organic nervous diseases occurring in the British Isles, multiple sclerosis now appears to be the commonest. The surveys of Northern Ireland and Northern Scotland show that in these parts of our islands at least one adult in every 13— is affected by it. The figure for England and Wales is probably only a little behind this one.

Secondly, there is a small but significant familial incidence varying in Great Britain from 5% to just over 10%. Since it is exceptional to find more than two members of a family, whatever its size, affected by the disease, it must be assumed that when present the genetic influence is usually weak and must be reinforced by constitutional or environmental factors before the nervous system is attacked, and furthermore, that the disease may develop in the absence of any obvious genetic influence.

Thirdly, in some patients a variety of factors, including ill health, an infection, trauma, and emotional stress may precipitate not only the onset of the disease, but also relapses.

The fourth fact about the disease concerns its abrupt onset and the natural tendency for symptoms to remit and later recur—features which for many years have been recognised as likely to provide a clue as to its ætiology.

Lastly, the considerable variation in the behaviour of the disease in its earlier stages must depend on the individual's reaction to it.

The Allergic Theory

For too long our attention has been fixed on the nervous system in multiple sclerosis. Detailed though the average history may be regarding events relating to this system, account is seldom taken of the recent and past general medical history. Yet it is in the medical background of these patients that we must look for the events which in a small proportion of the population initiate changes in the myelin sheath. Of recent views as to the cause of the disease, the so called allergic theory is perhaps the one most acceptable to the clinician. The occasional familial incidence; the nature and variety of the precipitating factors; the presence of some other form of allergy, before or after the onset, in a significant proportion of cases; an abnormal sensitivity to drugs d lastly the abrupt onset and characteristic relapsing d remitting course—all these factors may be cited in pport of the view that multiple sclerosis represents a pe of immunity reaction in the central nervous system cAlpine and Compston 1952)

Since confirmation or otherwise of this hypothesis ay be long delayed perhaps it is permissible to consider e nature of the hypothetical sensitising agent or agents. general allergens are derived from bacteria from otein derivatives and from drugs Since the breakdown oducts of bacteria constitute their commonest source, appears likely that, if sensitisation plays any part in he genesis of multiple sclerosis, an infection initiates he process, at least in some patients However, in ractice it would be difficult to prove such a relationship —first because of the time lag that might theoretically ccur between the infection and the first clinical evidence f the disease (McAlpine 1946) and secondly because s Rich (1947) has pointed out in discussing the question f allergy once a tissue has become sensitised it may bsequently react to a wide range of substances Support for the idea of a latent or asymptomatic phase of ultiple sclerosis comes from a consideration of the part layed by the so called precipitating factors. These are learly not strictly causal but in the words of Lumsden, 'either they fire off or trigger' an intrinsic self propagating mechanism, or they provoke the onset of symptoms n connection with areas of the white matter already nvolved by the disease process' (McAlpine Compston and Lumsden 1955) The second of these postulates eems probable and is consistent with the theory of llergy

Course of the Disease

This leads me to consider briefly certain features of arly symptomatology and the light they may throw on he nature of the initial change in myelin sheath Transitory and recurrent symptoms such as diplopia, blurred vision and paræsthesiæ, which in some patients may onstitute the earliest evidence of the disease, could be xplained on the basis of the so-called shadow plaque eferred to by Lumsden (1951) In this stage of partial demyelination it is not difficult to imagine that the nderlying axis cylinder might react abnormally to a variety of stimuli If the concept of an initial asymptomatic phase of the disease be accepted, does demyelination begin during this period or is there a stage of pre demyelination in which the complex cytochemical balance of the sheath is in some way altered?

In 1903 Williamson, of Manchester was struck by the similarity between the pattern produced by the application of a soluble dye to the cut surface of the spinal cord and the mode of development of plaques In 1933 Hallervorden and Spatz drew attention to the occasional occurrence of a ring formation in the early plaques of multiple sclerosis similar to that observed in Balo's concentric sclerosis. They attributed this type of formation to diffusion outwards from a central focus as in the so-called *Liesegang* phenomenon a subject recently discussed by Lumsden (McAlpine Compston and Lumsden 1955) The tendency for early symptoms particularly paræsthesiæ to spread according to contiguity of structure lends support to the possible rôle of a process of diffusion

The next question concerns the important issue as to whether arrest of the disease is ever possible For the pathologist this seems unlikely since plaques tend to evolve slowly and progressively On the other hand the clinician is aware of cases in which after one or more episodes no fresh evidence of the disease is apparent for many years and even in some instances for the rest of the patient's life Unless there is a system for following up early cases most of these patients will be missed for they may have no occasion to report either to their general practitioner or to hospital From my own observations I am satisfied that the incidence of these mild cases with a good resistance to the disease is rather higher than is generally supposed

It may be possible to reconcile these differing view points of clinician and pathologist The manner in which early symptoms clear up and may remain in abeyance for several years emphasises the potential reversibility or at least non progression of the early lesion; by contrast we are well aware of the probable course when paraplegic or cerebellar signs become established It is in this type of case that we can understand the evolution of the plaque as seen in the post mortem room

Treatment

Lastly brief reference must be made to the present unsatisfactory attitude towards treatment This attitude is determined by two beliefs—first that a serious degree of disability is inevitable in all cases however treated and secondly that treatment consists solely in palliative measures I have already pointed out that the *prognosis* as a whole is less unfavourable than was formerly thought and in some patients the disease runs a relatively benign course As regards treatment, the lack of an effective remedy should not blind us to the necessity of adopting a more positive attitude towards these patients, particularly in the early stage of the disease before irreversible changes in the nervous system have taken place Assuming that constitutional factors are important in the ætiology of multiple sclerosis, then it is our duty first to ensure an adequate period of rest in bed after the onset or a relapse followed by a long period of convalescence and secondly, to increase as far as possible the patient's resistance to the disease by close attention to physical and mental health over the first few crucial years

Owing to its capricious behaviour the *assessment of* treatment in multiple sclerosis has always presented difficulties. Yet the necessity of devising a *method of* evaluating a particular remedy is obvious Compston (1953) has suggested a formula by which the relapse rate before and after treatment can be compared. This method however does not cover the effect on recent symptoms

After consultation with Dr Richard Doll a form of trial has been devised in which a control group of patients can be used Briefly the trial is divided into two parts. The first enables a comparison to be made of the effects of treatment during a month's *stay in hospital* in two groups of patients one on the drug *under trial* and the other on some form of recognised treatment such as arsenic The object of the second trial is to assess the effect of the drug on the *relapse rate* It is hoped that experience gained during the next year will show the value of these two forms of trial

I would like to conclude with two observations The natural history *of multiple* sclerosis suggests that it is not due to a single cause but to the interplay of a number of factors—*genetic constitutional* and environmental Despite its complexity we *as neurologists* should not be content to leave this problem to the laboratory worker but with widened outlook should endeavour to play a part in its solution

REFERENCES

Allison, R S (1950) *Brain*, 73 103
— Millar J H D (1954) *Ulster med J* 23 suppl 2
Bing R. Reese, H (19 6) *Schweiz med Wschr* 56 30
Bramwell B, (1917) *Edinb med J* 18 16
Compston, N D (1953) *Lancet* ii 271
Curtius, F (1933) Multiple Sklerose und Erbanlage Leipzig
— Speer H (1937) *Z ges Neurol Psychiat* 160 226
Déjerine J (1884) *Rev med Paris* 4 193
Franklin C. R. Brickner R. M (194) *Arch. Neurol Psychiat Chicago* 58 125
Gram H C (1934) *Ugeskr Læg* 96 823
Hallervorden, J Spatz H (1933) *Arch Psychiat Nervenkr* 98 641.
Hoesslin von R (1934) Über Multiple Sklerose Munich.
Kershner M. (19 0) *Proc Ass Res nerv Dis* 28 632.
Kurland L. T (195) *Amer J Hyg* 55, 457
Lumsden C F (1951) *Brit med J* i 1035

References continued overleaf

A VALUATION OF HYDROCORTISONE OINTMENT

BRIAN RUSSELL
M.D Lond, F R C P, D P H
PHYSICIAN-IN CHARGE

J S PEGUM
M A Camb, M.D Lond, M R C P
ASSISTANT PHYSICIAN

N A. THORNE
M D Lond, M R C P
SENIOR REGISTRAR

R V GRANGE
M B Camb
REGISTRAR

SKIN DEPARTMENT, LONDON HOSPITAL

REPORTS from the United States and elsewhere indicate that hydrocortisone (17-hydroxycorticosterone, or compound F) ointment is highly effective in the treatment of various pruritic dermatoses

Sulzberger (1954) found it helpful in infantile eczema, atopic (prurigmous) dermatitis, contact eczematous dermatitis, otitis externa, nummular eczema, seborrhœic eczema, pruritus ani et vulvæ, exfoliative erythroderma of eczematoid or seborrhœic type, and some cases of eczematous and lichenified eruptions of the hands, feet, eyelids, face, neck, and genitalia, also in the "distinctive exudative, discoid, and lichenified dermatosis" of Sulzberger and Garbe Hydrocortisone has proved ineffective in pemphigus vulgaris, lichen planus, alopecia areata, psoriasis, and discoid lupus erythematosus, it does not inhibit the development of erythema from exposure to ultraviolet rays (Everall and Fisher 1952)

Alexander and Manheim (1953) and Malkinson and Wells (1954) have formed similar opinions, but they consider that hydrocortisone is ineffective in general exfoliative dermatitis, autosensitisation, and "-ide" (bacterial or fungous allergy) eruptions

McCorriston (1954), using hydrocortisone ointment in various vehicles, obtained 75–100% relief in 104 children and infants with eczema

Robinson (1953) obtained dramatic relief in 20 of 28 patients with atopic dermatitis, in 5 of 8 patients with pruritus vulvæ, and in 1 of 3 patients with pruritus ani 1 patient with discoid lupus erythematosus showed a good response and 2 showed fair responses

Sidi et al. (1953) state that the most striking effect is on pruritus, the action being immediate and lasting for at least twelve hours They used it for exogenous, allergic, seborrhœic, nummular, and purpuric eczemas, for pruritus, for chronic dermatitis of the eyelids, and for various other dermatoses

Goldman and Preston (1954) treated 22 cases of poison ivy dermatitis, with excellent results in 3, slight changes in 5, and no change in 14 cases

These reports suggest that hydrocortisone ointment relieves itching and reduces the manifestations of inflammation in a number of skin diseases, but in none of the above trials were concealed controls employed In the trial of any new treatment for pruritic conditions it is important to eliminate as far as possible the influence of suggestion, particularly when physical signs are slight and reliance has to be placed on subjective impressions

When anti histamine drugs were introduced, it was soon reported that they were effective local applications for the relief of itching Many of these claims were based on uncontrolled trials, on comparisons with previous remedies, or on trials which employed contralateral controls Later, Baldridge (1951) treated 41 patients with 5% phenindamine ('Thephorin') ointment on one side and its unmedicated base as a control on the other These were presented as "slightly different forms of the same medication" to the patients who were asked to estimate the percentage of relief on the two sides 47% of the areas treated with thephorin were reported as relieved, and 49% of the areas treated with the unmedicated base were reported as relieved Many dermatologists now agree that most anti histamine drugs are useless when applied topically

It can be said of contralateral controlled trials that at least four fallacies may invalidate the results

(1) Absorption may lead to remote as well as local effects

(2) The trial substance may inadvertently be transferred to the opposite side

(3) Unless the lesions on the two sides are of equal intensity and duration, they are not strictly comparable (e g, the response to treatment of an eczematide cannot be compared with that of the primary lesion—perhaps an area of unilateral hypostatic eczema—from which it developed) This difficulty can be overcome by random allocation of treatment and control to right and left sides, but even then, unless a large number of patients are included in the trial, the results may prove inconclusive

(4) There may be a *Mitreaktion* (Siemens 1951, 1953) in which, when a patch of skin disease is treated on one side of the body, untreated areas on the opposite side also show improvement This may be the result of a spinal reflex, or it may be accounted for by the reduction in the amount of circulating histamine which follows treatment

The Present Trial

In assessing the value of hydrocortisone ointment ('Hydro Cortisyl,' Roussel), we used concealed, alternating, self contained controls, the patients themselves recorded their daily progress over fourteen consecutive days on cards supplied to them each week

CONTROL BY ALTERNATION

A trial in which (*a*) the vehicle alone and (*b*) the substance being tested are used alternately in treatment has much to commend it, provided certain criteria are observed, and certain uncontrollable factors are appreciated

1 The number of patients tested in each group must be sufficiently large

2 The patient should be unaware that an ointment containing a trial substance is being tested against the ointment alone

3 The clinician should not know when the patient receives the trial ointment and when he receives the vehicle also until the specified period of the trial has been completed and all data have been recorded

4 It is possible that either substance will continue to exert some effect during the first few days after replacement by the other Thus the test remedy (or the vehicle alone) when applied during the second week may appear more (or less) effective than in the first week

5 The days of starting treatment should be evenly distributed through the week so as to spread the possible influence of weekends and bank holidays

6 The influence of menstruation is unlikely to be important if patients are introduced to the trial as they attend for treatment, without reference to the stage in the monthly cycle

7 If the whole trial covers several months, and preferably a year or more, and if patients enter it at various times, the influence of seasonal climatic changes is unlikely to important

8 The influence of extraneous factors such as fatigue, emotional disturbances, &c, may affect individual results Such factors should be noted at each attendance

9 Any record keeping by the patient is an abnormal state of affairs In suggestible patients results may prove better than might be expected, in very conscientious patients an increased awareness of attention to the skin may cause increased awareness of itching Both possibilities are likely, not only with the

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DR MCALPINE   REFERENCES—*continued*

McAlpine, D (1946) *Brain*, 69, 233
— (1954) Fifth International Neurological Congress, Lisbon
Comptes rendus 4, 198 *Arch Middx Hosp* n s 4 1
— Compston N D (1952) *Quart J Med* 21, 135
— — Lumsden C E (1955) Multiple Sclerosis Edinburgh
Müller, R. (1949) Studies on Disseminated Sclerosis *Acta med scand* suppl 222
Oppenheim H (1911) *Brit med J* ii 729
Pratt R. T C (1951) *J Neurol Psychiat* 14 326
— Compston N D McAlpine D (1951) *Brain*, 74, 191
Rich A R. (1947) Hypersensitivity in Disease *Harvey Lect*
Acta med scand suppl 137
1902–03) *Manchr med Rev* 4 4th ser 261

hicle but with the test substance as well Reciprocal short m trials are a useful means of determining the worth of a w remedy for chronic benign cutaneous reactions : the tient runs no risk and suffers no inconvenience if the hicle is harmless the vehicle may in fact prove helpful itself

THE RECORD CARDS

'Record of itching' cards adapted from cards used r Hodgkinson (1954) for controlled clinical trials of algesic drugs, were designed for the trial as follows

RECORD OF ITCHING

ate

atient s Name Record No

	Very good day (no itching)	Fair day (less itching)	Average day (usual itching)	Bad day (more itching)
un.				
lon				
'ue				
Ved.				
hu				
ri.				
at.				

Place X in appropriate space each morning for previous day

The patient s name and record number and the date were ntered by the clinician and a mark was made to show on hich day of the week the trial began. The patient s attention was then drawn to the request at the foot of the card Place X in appropriate space each morning for previous day " The ppropriate spaces recorded whether the patient had had a "very good day (no itching) a fair day (less itching) an "average day (usual itching) or a 'bad day (more itching)

The patients were unaware that two different preparations were being given to them They were informed that it was desired to find the worth of a remedy and that for this purpose a trial lasting two weeks was necessary No salesmanship ' was employed and the use of superlatives or of such adjectives as American ' and special' was avoided On the contrary, a restrained remark such as the following was made Please apply the ointment very thinly twice a day and record its effects on this card At the second attendance no matter what the result of the first week s treatment had been a comment was made such as the following A fortnight s treatment is needed to give the remedy a thorough trial It is best to have a fresh supply Please discard any ointment that remains and indicate results on this card for another week All patients coöperated well and seemed to understand what was required of them There were no 'spoiled papers.'

The method of prescribing was to write on the standard outpatient prescription card : HC ung trial 1st (or 2nd) week 5 g store no 1 The patients were told that only a small quantity of ointment could be provided for one week s treatment and they were sent to a special section of the outpatient dispensary This enabled concealed records to be made and kept by one pharmacist who was also responsible for arranging an approximately equal distribution between the A B (hydrocortisone→vehicle) and the B A (vehicle→hydrocortisone) trials He did this by alternating the A B and the B A sequence This resulted in a random distribution because there were eight different skin conditions included in the trial There were 66 patients in the A B sequence and 63 in the B A while 3 patients did not complete the trial We four clinicians had no means of telling which patients received the A B and which the B A sequence because we did not know when one of us had introduced a new patient to the trial—or for that matter the order in which the patients arrived at the dispensary 5 g of ointment or base was dispensed as a rule but sometimes 10 g was given The control ointment (of propylene glycol polyethylene glycols, and zinc stearate) was the same as the vehicle for the 2 5% hydrocortisone acetate ointment ; the two ointments were identical in appearance Identical plastic ointment boxes were used for the trial substance and for the base They were not labelled in any way to indicate the nature of the contents At the end of each fortnight s trial the pharmacist was asked to divulge the treatment that had been given each week, so that a decision might be made on the future treatment of that patient Progress notes were also made at each attendance, the patient s verbal descriptions being recorded , these made a valuable parallel study to the record cards. Changes in physical signs were also recorded.

In some of the conditions—e.g anogenital pruritus—physical signs were often slight or absent the changes being mainly or entirely subjective In patients with multiple lesions—e.g some cases of discoid eczema—the trial ointments had to be applied to one area only, while the remaining lesions were treated with some other bland local application As far as possible sedatives were withheld during the trial period if they were necessary, they were given for both weeks in identical doses

On inspecting both cards and after allowing for carry over effects it was usually easy to decide which preparation was the more effective The subjective results recorded during the last day or two of a week s trial were often poorer than during the middle of the week. We believe that this was often due to the necessity for very sparing use of the ointment towards the end of each week because of the small amount (5 g) that was usually supplied

In cases where the 2 5% hydrocortisone ointment proved more effective than the base alone treatment was continued with 1% hydrocortisone ointment Sometimes treatment was continued with the base and a change-over to 2 5% or 1% hydrocortisone ointment was made after a further week or two without the patient s knowledge It was thus possible to clarify inconclusive impressions gained from the first trial. It was also possible to compare the efficacy of 2 5% with 1% hydrocortisone ointment ; sometimes the 2 5% preparation was necessary for complete control in others 1% was sufficient

MATERIAL

Included in the trial were 132 patients (72 males and 60 females), with the following conditions

25 with anogenital pruritus
21 with lichen simplex.
12 with infantile eczema.
22 with Besnier's prurigo
23 with discoid eczema
11 with chronic idiopathic eczematous dermatitis of the hands
11 with otitis externa
7 with pruritic psoriasis mostly anogenital

RESULTS

Points were allotted daily to each patient studied allowing 2 points for complete relief, 1 for partial relief 0 for no change, and –1 for worsening These numerals indicate trends only and in no way imply degrees or percentages of relief The points scored are recorded on block diagrams in figs 1–8 These show great individual variations of subjective relief We have thought it valid to summarise the effects obtained in 'hydrocortisone" and vehicle' groups during the week of their application The daily means are set out in table I.

The number of patients in a few of the groups was too small for dogmatic statements but it is clear from this table that appreciably greater improvement sometimes resulted from the use of hydrocortisone No absolute criterion of efficacy can be applied but on the above rating the results may be summarised thus :

Lichen simplex discoid eczema and otitis externa.—The results were strongly in favour of hydrocortisone

Infantile eczema and idiopathic eczematous dermatitis of the hands.—The results though apparently in favour of hydrocortisone, were less conclusive

Pruritic anogenital psoriasis—The results were equivocal In the course of treatment with hydrocortisone ointment 6 patients improved and 1 worsened, while with the vehicle alone 5 patients improved and 2 worsened This suggests that the vehicle was responsible for the improvement

Besnier's prurigo—Slightly better results were obtained with the vehicle alone, but neither hydrocortisone nor the vehicle produced very good results Undoubtedly the trial was often inadequate in this condition, because the cost and scarcity of hydrocortisone made it advisable to use it only on the worst, lichenified areas in these patients Nevertheless, clinical and electro encephalographic evidence (Ingram 1955, Russell and Last 1955) indicates that this disease affects the whole ectoderm (nervous system and skin), so it is not surprising that local treatment by itself should prove ineffective

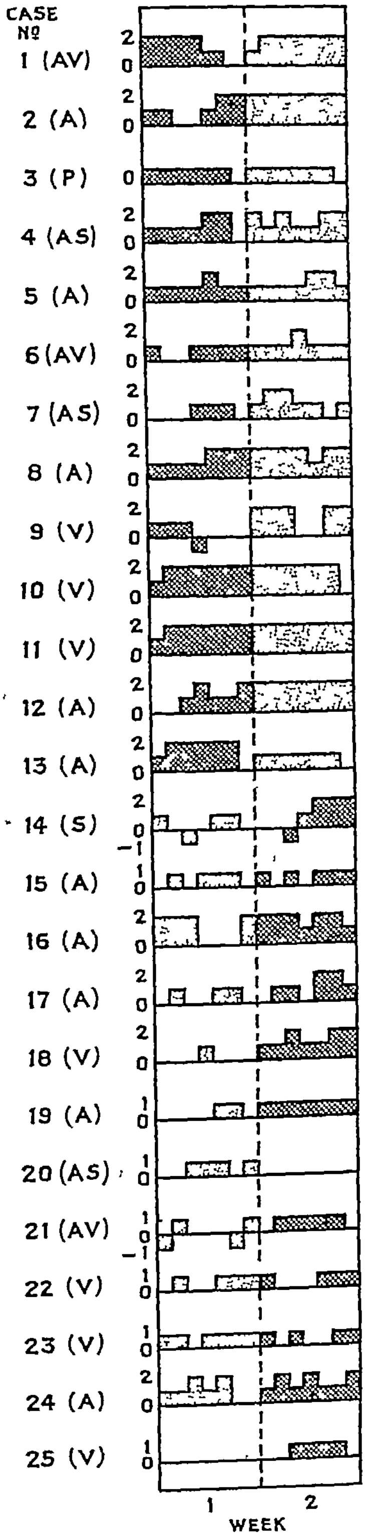


Fig 1—Results in 25 cases of anogenital pruritus.
A = anal P = perineal
S = scrotal V = vulvar

Anogenital pruritus—Slightly better results were obtained with the vehicle alone Nevertheless excellent longer term results were obtained in this condition with hydrocortisone (see below), 32% of patients being completely relieved and another 24% much improved We can only suggest that our equivocal findings in the "switch over" trial were due to one or more of the following factors the shortness of the trial, the undoubted efficacy of the vehicle itself, the carry over effects from one week to the next, and, in some cases, the influence of suggestion There was no obvious difference between the results obtained in anal pruritus and in genital pruritus Patients with distinct physical signs—chiefly lichenification—responded best, and those without physical signs responded worst This is not surprising, for pruritus without physical signs is probably of central origin

SIDE-EFFECTS FROM HYDROCORTISONE OINTMENT

Remote Effects

We have seen no evidence of remote ill effects following the use of hydrocortisone ointment

Smith (1953) found no significant change in the eosinophil count after the inunction of 6 g of 2 5% hydrocortisone-acetate ointment, and he thought it unlikely that amounts of hydrocortisone so small as to escape detection could account for the therapeutic effects reported No systemic ill effect has been reported from the prolonged application of hydrocortisone ointment.

Local Irritation, Sensitisation, and Aggravation of Infective Dermatoses

In the series of Malkinson and Wells (1954) irritation developed in 4 of 71 patients treated, and the treatment was stopped, but no case of sensitisation to hydrocortisone has yet been reported There were no cases in our series 3 of Robinson's (1953) patients complained of increased burning and itching when the ointment was applied, and 2 of them were found to be sensitive to the lanolin in the ointment base The ointment used in the present trial did not contain lanolin A few of our patients stated that it was "too drying," but the great majority found it comforting and aesthetically acceptable The occasional complaint of undue dryness can be overcome by having an alternative vehicle of hydrous ointment type, but the routine use of a greasy vehicle of this sort would be liable to cause maceration of the skin at some sites

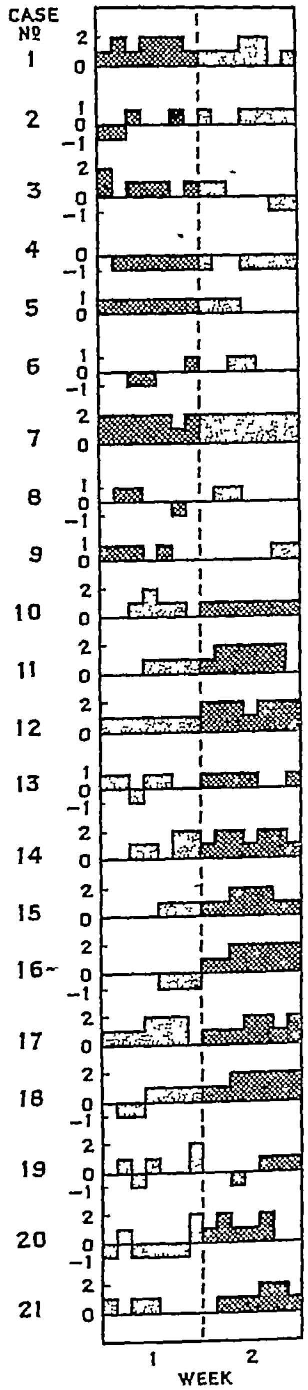


Fig 2—Results in 21 cases of lichen simplex

3 of our patients abandoned the treatment and were not included in the tabulated results They were

1 A patient with discoid eczema who complained that the ointment "burned" She was receiving the vehicle alone at the time She refused to attend again for patch testing, on the grounds that the dermatosis had cleared up with treatment for her "nerves"

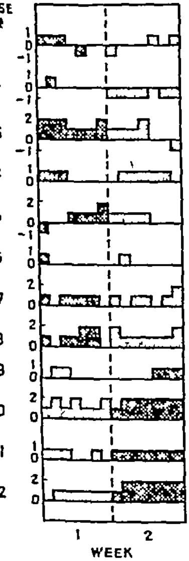
2 A patient with chronic eczematous dermatitis of the hands, of unknown cause who complained of fresh outcrops of vesicles after applying hydrocortisone ointment for three days She abandoned its use Patch tests with the hydrocortisone ointment and with the vehicle alone were negative, but when patch testing was carried out with the separate constitutents of the vehicle, a positive response was obtained to propylene glycol Her dermatitis subsequently improved

KEY TO FIGS 1–8.

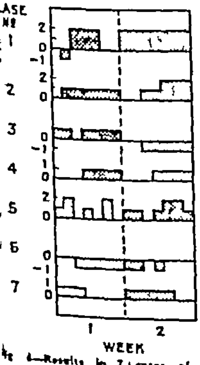
Hatched = hydrocortisone. Stippled = vehicle 2 = no itching 1 = diminished itching 0 = usual itching -1 = increasing itching lly when 2·5% hydrocortisone, with hydrous ointment as vehicle was applied. This had been specially prepared ur request.

A patient with otitis externa, whose ears became more len and exudative shortly after he began treatment with rocortisone ointment. His eyes also became swollen Cul revealed *Staphylococcus pyogenes streptococcus hæmolyticus Pseudomonas pyocyanea* Patch tests with hydrocortisone with the vehicle were negative

Malkinson and Wells (1954) did not find that secon lly infected dermatitis was aggravated by the drug The anti inflammatory action of hydrocortisone relieves itching and lessens scratching, thus diminishing bacterial contamination of the lesions and bringing about amelioration of the infective as well as of the eczematous and lichenified elements On the other hand, dermal infections with cocci (such as erysipelas boils, and ecthyma) should in theory be aggravated by hydrocortisone which has the effect of lowering the resistance of the host thus enabling the organisms to multiply (Houghton 1954 Hart 1954) This matter is still sub judice



g 3—Results in 12 cases of infantile eczema



g 6—Results in 7 cases of pruritus of anogenital region.

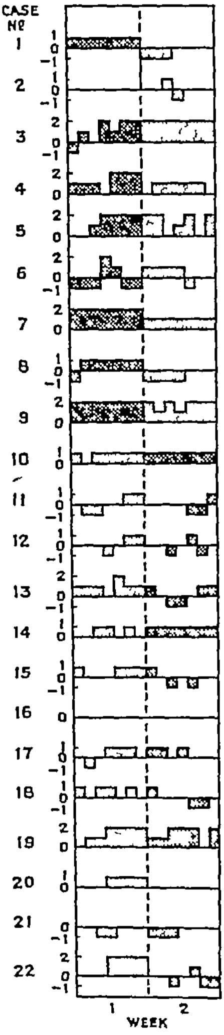


Fig 4—Results in 22 cases of Besnier's prurigo.

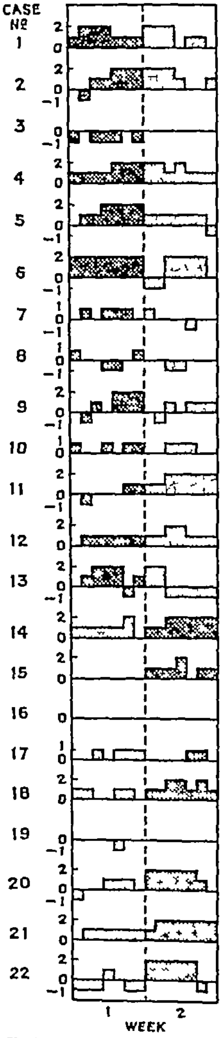


Fig 5—Results in 23 cases of discoid eczema. The 23rd patient failed to complete the trial.

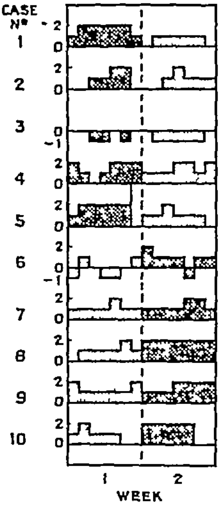


Fig 7—Results in 11 cases of otitis externa. The 11th patient failed to complete the trial.

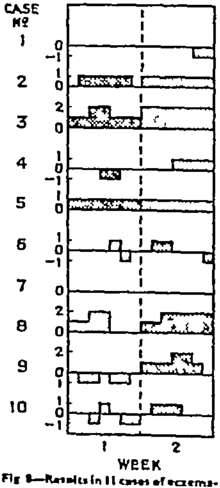


Fig 8—Results in 11 cases of eczematous dermatitis of hands. The 11th patient failed to complete the trial.

TABLE I—MEAN DAILY RESPONSE SCORES

Diagnosis	No of cases	Score with hydrocortisone	Score with vehicle
Anogenital pruritus	25	1 01	1 04
Lichen simplex	21	1 00	0 49
Infantile eczema	12	0 84	0 55
Besnier's prurigo	22	0 54	0 59
Discoid eczema	23	0 97	0 57
Idiopathic eczematous dermatitis of the hands	11	0 61	0 43
Otitis externa	11	1 28	0 79
Pruritic anogenital psoriasis	7	0 63	0 51

EFFICACY OF THE VEHICLE

In trials such as this it is always possible that the bland vehicle may have a considerable antipruritic action

Sulzberger and Witten (1952), in their early trials of hydrocortisone, noted some improvement with the ointment base alone, though less than with the ointment containing hydrocortisone McCorriston (1954), too, noted that in a number of patients *the control sites of the soft paraffin and emulgent* bases showed some improvement This was confirmed in a later study by Sulzberger et al (1953) Most of their patients were treated with hydrocortisone acetate in a non greasy base (containing zinc stearate, propylene glycol, polyethylene glycols, and water)

Robinson (1953) noted that after the condition had been *controlled by hydrocortisone, it often seemed to respond* better to other local therapy than previously

McCorriston has used hydrocortisone in four different vehicles in the treatment of infantile eczema These were a cream of zinc stearate, propylene glycol, polyethylene glycols, and water, white soft paraffin, a jelly base, and an oil in-water emulgent base Though the cream was useful in the *weeping stage, the jelly was found to be too drying* The soft paraffin or the emulgent base were preferable for dry, thick, scaly areas

In the present trial the vehicle was similar to that used by Sulzberger and Witten (1952)—namely, a non greasy polyethylene glycol base Polyethylene glycols *(Smyth et al 1950) have proved less irritant than soft* paraffin mild sensitisation reactions (faint erythema) as almost as common as with lanolin, soft paraffin, simple cerate, and simple ointment Case reports of sensitivity to polyethylene glycols are very few Strauss (1950) reported 2 cases of sensitivity to the entire group of polyethylene glycols These substances are non-ionic (Schutz 1953), they are therefore insensitive to metallic ions, and can be used both in acid and in alkaline media They dissolve or emulsify lipophilic substances and are valuable vehicles for oil soluble drugs when it is desired to bring these *into close contact* with the skin and with its folds

Results obtained with the vehicle in the present study *indicate that it is* remarkably effective by itself as an emollient and as an antipruritic agent, but its efficacy is far less than that of hydrocortisone ointment in of the skin diseases that we have studied

From the cosmetic point of view, a non greasy b of the " vanishing " type is more pleasant than a greasy *ointment* We agree with Sidi and Bourgeois Gavardi (1953) that the polyethylene-glycol base has an action superior to that of most local applications, and it has the advantages of *being æsthetically* acceptable and not necessitating dressings

TABLE II—INDEPENDENT ASSESSMENT OF EFFECT OF HYDROCORTISONE OINTMENT

Disorder	Cleared without relapse	Completely controlled	Much improved	Slightly improved	Unchanged	Worse or course abandoned
Anogenital pruritus	2	6	6	8	2	1
Lichen simplex	0	2	8	3	7	1
Infantile eczema	0	2	0	6	4	0
Besnier's prurigo	0	2	1	7	11	1
Discoid eczema	2	3	4	4	9	1
Idiopathic eczematous dermatitis of the hands	0	1	2	1	5	2
Otitis externa	2	3	2	2	1	1
Pruritic anogenital psoriasis	1	0	1	1	4	0
Total	7	19	24	32	43	7

SUBSEQUENT PROGRESS

With more prolonged treatment (without concealed control or record cards) progress has been maintained in lichen simplex, discoid eczema, anogenital pruritus, and otitis externa As extraneous events have a powerful influence on progress in infantile eczema, hydrocortisone ointment, though often helpful, may have to be assisted by sedative drugs In cases of Besnier's prurigo we *have not felt* justified in continuing treatment with hydrocortisone

INDEPENDENT ASSESSMENT

An independent observer (Dr C M Ridley) has perused the case notes and analysed the results The assessment (table II) was made on subjective impressions combined with the objective evidence recorded in the notes, it attempted to measure the effect from the beginning to the end of treatment with hydrocortisone ointment The duration of treatment varied from two weeks to several weeks In some cases treatment with hydrocortisone ointment was still in progress at the time of the assessment

CONTACT ECZEMATOUS DERMATITIS

We have observed marked relief of contact eczematous *dermatitis with hydrocortisone* ointment However, the condition does not lend itself to controlled studies, its natural course differing greatly from one person to another

Summary

Concealed trials with hydrocortisone ointment, alternated with its vehicle alone, and a longer term independent survey of results, have shown that hydrocortisone was remarkably effective in many patients with lichen simplex, discoid eczema, otitis externa, and anogenital pruritus In infantile eczema and in idiopathic *eczematous dermatitis of the hands* the improvement was less obvious In Besnier's prurigo local improvement was sometimes obtained, but the general results were poor one reason for this may have been that the ointment applied in very small quantities In itchy psoriasis of the anogenital region the results *apparently depended* on the efficacy of the vehicle

Hydrocortisone ointment is also highly effective in contact eczematous *dermatitis*, but examples of condition have not been included in these controlled

An independent observer, assessing the results, concluded that there had been distinct or complete relief in 14 of 25 patients with anogenital pruritus, in 10 of with lichen simplex, in 2 of 12 with infantile ec in 3 of 22 with Besnier's prurigo, in 9 of 23 with di eczema, in 3 of 11 with idiopathic eczematous derm *of the hands, in 7 of 11 with otitis* externa, and of 7 with itchy flexural and genital psoriasis

Only 1 of the 132 patients in the trial proved sensitive to the vehicle, but relief was subsequently obtained with hydrocortisone in hydrous ointment 1 patient complained *that the ointment caused* a burning sensation in another infection increased during treatment

We wish to thank Dr L Bernstein, of the department of physiology of the London Hospital, for his statistical guidance and constructive criticism, and Dr A E Gremeaux, of Roussel Laboratories, for his coöperation, and for supplying the hydrocortisone ointment and the inert vehicle which we

in the trial We also thank Mr D C Phillips of the maceutical department of the London Hospital, who onally supervised the concealed trial

REFERENCES

ander R. M., Manheim, S D (1953) *J invest. Derm.* 21 223
ndge G D (1951) *Arch Derm Syph Chicago* 63 260
all, J., Fisher L (195?) *J invest Derm.* 19 97
man, L Preston R. H (1954) *J Amer med Ass* 154 1318
P D A (1954) *Brit med J* ii, 768
ckinson, R. (1954) Therapeutic Notes (Parke Davis) no 3 p 7
ghton L E (1951) *Lancet*, i 695
am, J T (1955) *Brit J Derm* 67 43
orriston, L. R. (1954) *Canad med Ass J* 70 59
dnson, F D., Wells, G C. (1954) *Brit J Derm* 66 300
inson, R. O. V (1953) *Bull Johns Hopk. Hosp* 93 147
ell, D., Last, S L (1955) *Brit. J Derm.* 67 65
itz, E. (1953) *ArzneimittelForsch* 3 451
, E., Bourgeois-Gavardin, J (1953) *Pr méd* 61 1700
— — Plas, G (1953) *Ibid* p 99?
ms, H W (1951) *Hautarzt* 2 430
— (1952) *Ibid* 3 463
th C. D (1953) *Arch Derm. Syph Chicago* 68 50
th H F jun., Carpenter C. P Weil C S (1950) *J Amer pharm. Ass.* 39 319
ms, M. J (1950) *Arch. Derm. Syph. Chicago*, 61 420
berger, M B., (1954) *In* Modern Trends in Dermatology Edited by R. M. B MacKenna London
— Witten, V H (1952) *J invest Derm.* 19 102
— — Smith, C C. (1953) *J Amer med Ass* 151 6

STOCHEMICAL OBSERVATIONS ON THE SUPRARENAL GLANDS IN CHOLERA

S N De
M.B Calcutta Ph.D Lond D T.M.
PROFESSOR OF PATHOLOGY

K P Sengupta
M B Calcutta
CURATOR, PATHOLOGICAL MUSEUM

N C Ganguli
M.B Calcutta
RESEARCH ASSISTANT *

PARTMENT OF PATHOLOGY NILRATAN SIRCAR MEDICAL COLLEGE, CALCUTTA

Cholera, a disease characterised by loss of fluid ered blood volume shock and anoxia appears to be ideal condition for the study of Selye s (1950) alarm action in man However very little is known about e activity of the suprarenal glands in cholera

Rogers (1921) citing Nearne considered the high tolerance cholera patients to adrenaline as an indication of suprarenal sfunction.

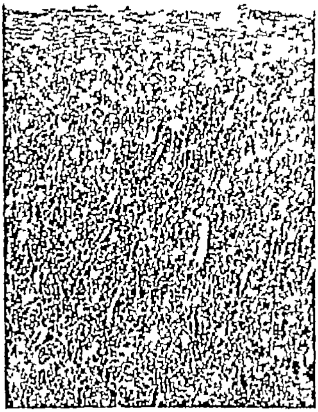


Fig. 2—Suprarenal gland in cholera showing complete depletion of sudanophil material (no black stain) Details as in fig 1

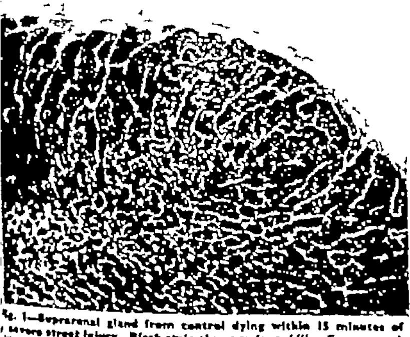
Chatterjee (1930) studied the suprarenal glands from some cases of cholera and thought the congestion of boundary zone to be related to the extreme shock of the first stage of the disease

Lahiri (1946) treated a few cases with total suprarenal cortical extract and noted some improvement of the vascular tone

We have in the past searched in vain for any significant morphological change in the suprarenals in cholera by ordinary staining methods The recent paper by Stoner et al (1953) prompted us to try their histochemical methods on our cholera materials. A preliminary report of our findings was read at the fifth annual meeting of the Indian Association of Pathologists

Materials and Methods

We studied eleven pairs of suprarenal glands from bacteriologically positive cases of cholera fatal within 48 hours after onset in the stage of shock Ten pairs of glands from patients dying within 15 minutes of injuries from street or railway accidents served as controls None of the patients was aged less than 10 years and the controls showed no gross pathological changes except those of their injuries The necropsies were done 24–48 hours after death on bodies kept in the cold chamber Five frozen sections from different blocks of each gland were prepared for the detection of neutral fat by staining with Sudan iv, of cholesterol with digitonin seen by polarised light and of ketosteroids with 2 4 dinitrophenylhydrazine No attempt was made to ascertain the weights of the glands the thicknesses of different zones or the cell-size



g. 1—Suprarenal gland from control dying within 15 minutes of a severe street injury Black stain shows sudanophilia. Frozen section 20 µ thick. (Sudan IV × 70.)

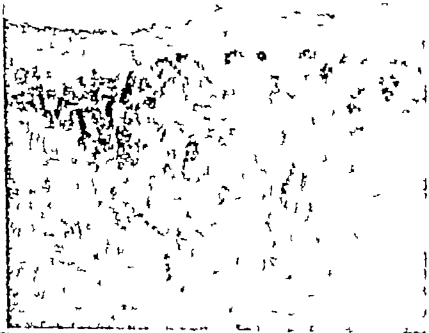


Fig 3—Suprarenal gland in cholera, showing small sudanophil islets retained. Details as in fig 1

Under the auspices of the Indian Council of Medical Research

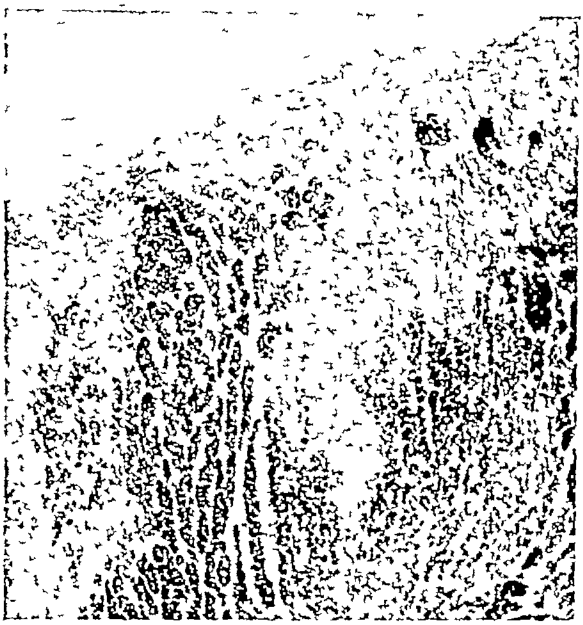


Fig 4—Patchy disappearance of sudanophil material in suprarenal gland in cholera. Details as in fig 1

Results

In four cases there was evidence of complete depletion of neutral fat from all the zones (figs 1 and 2) Only an occasional cholesterol crystal could be made out here and there Staining for ketosteroid showed a faint pale yellow coloration

In five cases neutral fat was seen to have disappeared in patches of varying extent—either wide areas still retained it, or wider areas had only small islands of it left here and there (figs 3 and 4) In one case loss of neutral fat was confined to the zona glomerulosa (fig 5) This patient received only $1^1/_2$ pints of saline solution before he died, in contrast to 4–38 pints received by other patients in 1–3 days In all these cases ketosteroid and cholesterol showed patchy distribution, but evidence of depletion of cholesterol was much more striking (figs 6 and 7)

In the 11th case all the zones retained sudanophil material while cholesterol crystals were confined to the zona glomerulosa only (fig 8)

One constant finding was that, whereas the neutral fat in the *control glands* appeared large and globular, that seen in cholera was always smaller and granular (figs 9 and 10)

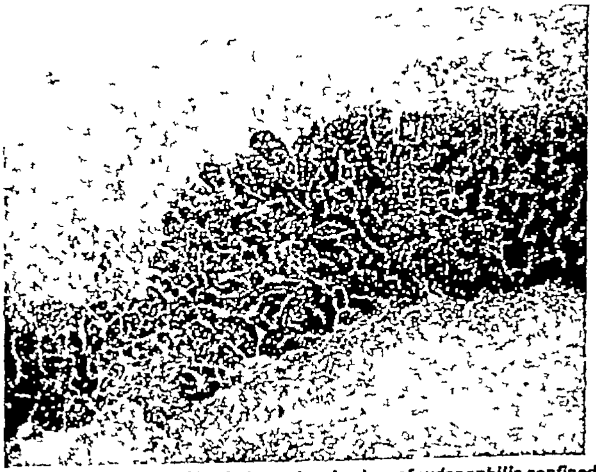


Fig 5—Suprarenal gland in cholera, showing loss of sudanophilia confined zona glomerulosa. Details as in fig 1

Discussion

This histochemical evidence of depletion of lipoid material has generally been thought to be associated with increased liberation of cortical hormone under various conditions Selye (1950) has described similar changes in his experiments on animals with non-specific alarm reaction and has related them to increased activity of the suprarenal glands under stimulation of the adrenocorticotropic hormone of the hypophysis Histochemical reactions have recently been used to investigate the functional state of the gland, but there is no agreement about their specificity Particular importance has been attached to the cholesterol content and its relative distribution An inverse correlation between *cholesterol content and secretory activity of the gland* has been well established by using stimuli of varying intensity and duration Sayers (1950) regards cholesterol as the precursor of cortical hormone, large stores being held in the suprarenal glands in readiness for emergency periods requiring enhanced synthesis of the hormone We have not estimated the cholesterol content of the glands but have attempted to form an idea from the above mentioned histochemical test, and there is good evidence that it tends to disappear in cholera Staining for ketosteroids may give an idea of the relative amount of the finished hormone available at the moment, but the significance of sudanophil material is not clear. A correlation between change in these lipoids has not always been possible, and Sayers (1950) thinks it is due to slight differences in technique We have, however, found a broadly parallel change in these three materials, although sometimes traces of cholesterol were left when neutral fat and ketosteroid had disappeared, or no cholesterol could be seen in the zona fasciculata, where sudanophil material still persisted Depletion of steroid has, however, been often greater than that of sudanophil material Ayres et al (1951) noted the same in acute infections

Fig 6—Birefringent crystals of digitonin cholesterol seen in polarised light suprarenal gland from control. From section 25 µ. (× 70)

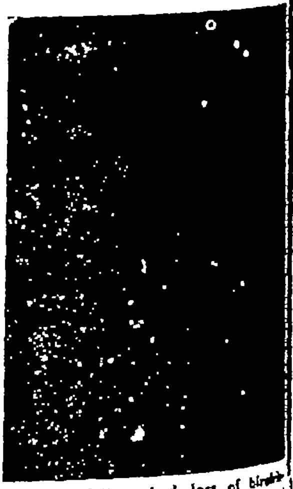


Fig 7—Well marked loss of birefringent crystals from suprarenal gland in cholera. Details as in fig 6.

In one case the zona glomerulosa was depleted of all lipoids, and in another this zone alone showed crystals f cholesterol. The former patient received only $1^{1}/_{2}$ ints of saline solution during his short stay in the ospital, and the latter received 24 pints in 46 hours It s tempting to think that the zonal picture in the two ases was caused by hyponatræmia in the former and ypernatræmia in the latter It should, however, be emembered that the blood sodium level was not stimated in any of these cases that only two such cases ere observed and that the question of zonal autonomy ill remains an enigma (Sayers 1950) so it will be rash o draw any conclusion from this observation

The over-all picture seen in cholera suggests that the uprarenal glands play an active rôle in cholera by nhanced synthesis of its hormonal products This oncept finds support in another recent observation in his laboratory (De et al. 1955) on the hæmatological hanges in untreated cases of cholera Cholera is not ssociated with suppuration or emigration of leucocytes nywhere into the tissues, yet the blood shows a leucocytosis which is much more than can be explained by imple hæmoconcentration At the same time there are eutrophilia lymphopenia, and eosinopenia Not only re the eosinophils diminished but in many cases they eem to disappear altogether from the peripheral blood. ll these facts are generally regarded today as convincing evidence of increased suprarenal cortical activity

As regards the relation of *Vibrio choleræ* or its products o these various changes, similar blood changes have been ound in our vibrio negative cases Besides, no sign of ecrosis or hæmorrhage has been seen in the suprarenal glands of cholera patients. These facts suggest that all he changes in the blood and in the suprarenal glands form art of a non-specific response on the part of the body to he associated dehydration shock and anoxia

ig. 8—Birefringence confined to zona glomerulosa in suprarenal gland of cholera patient treated with large doses of saline solution. Details as in fig. 6.

Be that as it may the functional capacity of the drenal cortex, judged by the histochemical techniques oes not appear to be the same in all these cases of holera at the time of death In four cases there was omplete depletion of all lipoids—regarded by Stoner t al (1953) as evidence of complete exhaustion Cortical ailure may reasonably be suspected in these cases though ot proved. In the others variable amounts of lipoid re still left indicating that the glands retain some tock of basic elements for responding to further corticotropic stimulation In spite of such potent suprarenal lands, cortical hormonal deficiency may have been esponsible for the fatal outcome when the failure may e located at a supra adrenal level

Sevitt (1954) used a combination of adrenaline and orticotrophin tests in fifty four cases of burns and iagnosed adrenocortical failure in five and failure of he pituitary-adrenal axis in two cases Cortisone therapy as indicated in the former and corticotrophin in the atter To clarify the therapeutic implications of our bservations in cholera further investigations into the unctional state of the two units of the pituitary suprarenal axis by serial blood-counts with these special methods up to the time of death will be necessary

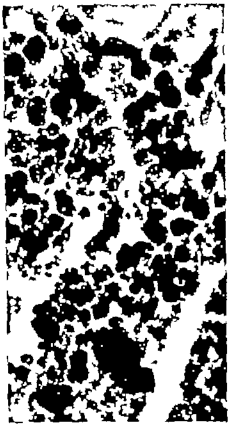


Fig. 9—Sudanophil globules in control suprarenal gland. Details as in fig 1 (× 250)

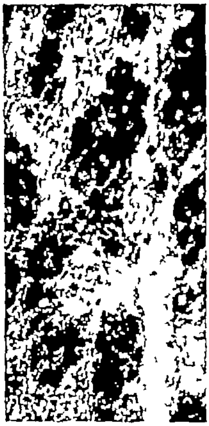


Fig 10—Sudanophil granules in suprarenal gland in cholera. Details as in fig 1

Conclusions and Summary

Evidence of various degrees of depletion of cortical lipoids suggests an active rôle of the suprarenal cortex for enhanced synthesis of its hormones in response to the stress of dehydration, shock, and anoxia of cholera

Further work to inquire into the functional state of the pituitary suprarenal system in cholera is called for

We wish to thank Dr A K. Duttagupta for permission to publish and Mr M Mazumder for the photomicrographs.

REFERENCES

Ayres, W W Firminger H. I Hamilton P K. (1951) *Milit Surg* 109 603
Chatterjee, H N (1939) *Calcutta med J* 36 165
De, S N Bose S N Mondal A (1955) To be published.
Lahiri, S C (1946) *J Indian med. Ass* 14 113
Rogers L (1921) Bowel Diseases in the Tropics. London p. 198
Sayers G (1950) *Physiol Rev* 30 241
Selye, H (1950) The Physiology and Pathology of Exposure to Stress Montreal
Sevitt, S (1954) *Brit. med. J* 1, 541
Stoner H B., Whitley H J Emery J L (1953) *J Path Bact* 66, 171

CLINICAL EXPERIENCES WITH
SOFT-TISSUE PLACENTOGRAPHY

ROBERT PERCIVAL
F.R C.S M.R C O G
OBSTETRIC SURGEON

STANLEY MURRAY
M.D Belf F.R C.S.I., D.M.R
ASSISTANT RADIOLOGIST

THE LONDON HOSPITAL

OUR object is to draw attention again to the advantages of soft tissue placentography which in our experience, has proved a safe and reliable way of establishing the position of the placenta

The work of Reid and of Whitehead on the radiological aspects of soft tissue placentography should leave no doubt as to its reliability simplicity and safety But essential for success is close collaboration between radiologist and obstetrician with interest and confidence equally distributed.

The method is valuable for several reasons. Firstly, the position of the placenta can almost always be seen or be deduced without any other examination It is not disturbing to the patient and in selected cases it may be used for outpatients Secondly it saves beds. Now that antepartum hæmorrhage is managed conservatively patients may have to stay in hospital for as long as six weeks before the fœtus is judged mature enough to risk premature delivery after examination under anæsthesia Soft tissue placentography can greatly reduce such use of valuable beds in non-toxic antepartum hæmorrhage, once placenta prævia has been excluded and bleeding has ceased the patient can safely be sent home Thirdly, it saves patients from wasting time unnecessarily in hospital No longer need a patient who has bled a little at 32 weeks, but is otherwise normal, be kept in hospital for weeks If bleeding is very slight or has stopped, it is quite easy to decide the position of the placenta within half an hour of the patient's admission It cannot be denied that up to the 34th week of pregnancy the method is not always as accurate as it is after this time, this applies to the borderline case in which the placenta appears to dip just beneath the brim, especially when it is anterior Radiography two weeks later will often show the placenta wholly above the brim, as if it had risen as the lower segment became more differentiated Finally, soft tissue placentography is a useful means of finding out whether the position of the placenta, even when in the upper segment, is responsible for a particular presentation or lie (Stevenson 1951) Moreover, it often explains why version has not been successful, and if a second attempt at version is made the dangerous placental site can be avoided

Recent Work

Chief credit for redirecting attention to this essentially simple technique must go to Reid (1949) and Whitehead (1953) The methods involving artificial-contrast media (amniography, cystography, and intravenous placentography) have been examined thoroughly by these workers, who found that they lacked simplicity and accuracy and accordingly were unsuitable for routine use Reid and Whitehead independently followed the lead of Snow and Powell (1934) and others, by making the fœtus serve as its own contrast medium and by deducing the position of the placenta from its displacement of the fœtus The need for such a technique was emphasised when Moir (1944) proved that the uterine wall, the liquor amnii, and the placenta have identical radiographic density, and that consequently no hope could be held out for ordinary soft-tissue methods in locating the placental site

In addition to the valuable radiographic density of the fœtus, use is made of another of its properties—its molecular density, which is greater than that of the fluid surrounding it The fœtus sinks to the lowest point of the amniotic cavity, and by changing the patient's position any area of the uterine wall can be examined against the outline of the fœtus

Clinical Indications for Placentography

275 cases were studied over the three year period 1951–53 At first the patients were carefully selected, but when we became more familiar with the technique we used it more widely During the early part of the trial the method was not used by every member of the unit, so the series cannot be said to include all examples of the different clinical problems which we investigated After the first six months all patients suspected on clinical grounds of having placenta prævia were submitted to placentography The following list gives an idea of the type of case where we considered it an advantage to discover the position of the placenta

(1) Antepartum hæmorrhage, where the precise diagnosis is in doubt
(2) Unexplained displacement of the presenting part
  (a) High head
  (b) Recurrent malpresentation.
(3) Cases of (1) and (2) combined
(4) Unexplained breech presentations
(5) Unexpected failure of version
(6) Cases due for surgical induction (especially by the Drew Smythe catheter) in which the presenting part is unengaged
(7) Other indications

(1) *Antepartum hæmorrhage, where the precise diagnosis is in doubt*

This is by far the most important indication. When local causes have been excluded there remain, for practical purposes, only two conditions to differentiate—accidental hæmorrhage and placenta prævia Placentography will immediately indicate the position of the placenta There are other signs of diagnostic value when the placenta occupies the lower segment, especially in the last few weeks of pregnancy, but before this the presentation is not expected to be stable, and it is in these very cases, especially when the placenta is on the anterior wall, that physical signs are equivocal and placentography is of the greatest value

Again, bleeding thought to be caused by toxæmia may in fact be due to placenta prævia In this series the combination of toxæmia with placenta prævia was found only twice, and in neither instance was there any evidence of accidental hæmorrhage Bender (1953), on the other hand, found that toxæmic accidental hæmorrhage accounted for the bleeding in 10 of 102 cases of placenta prævia

(2) *Unexplained displacement of the presenting part*

(*a*) *High head*—In the last few weeks of pregnancy, if the head is high and it cannot be pushed into the pelvis, and if no other cause is found, then placentography would be helpful

(*b*) *Recurrent malpresentation*—The indications here are similar Stevenson (1951) has emphasised the high incidence of a completely fundal or lower-segment location of the placenta in persistent transverse lie

(3) *Case of (1) and (2) combined*

One would expect to find placenta prævia in these circumstances, yet of 38 cases of antepartum hæmorrhage associated with high head or unstable presentation only 13 had placenta prævia, in the remaining 25 the placenta was situated normally One of the criticisms levelled at radiological placental localisation has been that with placenta prævia the diagnosis can be made by abdominal examination Undoubtedly experience and an intelligent application of clinical methods will result in relatively few mistakes The patient who is known to have bled is of course admitted to hospital, but if she has not the obstetrician may become dangerously complacent unless an easy and accurate means of detecting a placenta prævia is available Moreover, the very knowledge that unexplained non engagement of the head can exist in the absence of placenta prævia may provide a ready excuse for not investigating further, and so defeat the most effective means of lowering the fœtal and maternal death rate from placenta prævia—namely, that of diagnosing it and admitting the patient to hospital before any bleeding has taken place

(4) *Unexplained breech presentations*

Stevenson (1951) has shown that the commonest site for the placenta in persistent breech is the uterine cornu, and he has suggested that this causes such alteration in the shape of the uterine cavity that the fœtus is accommodated more readily as a breech In the few cases investigated we have confirmed the preponderance of the cornual position and have found placenta prævia relatively infrequently (table III)

(5) *Unexpected failure of version*

It is not uncommon to fail unexpectedly to turn a breech that has been judged suitable for version, even after it has been disengaged There are probably several reasons for this, but the most likely is that the bulk of the cornual placenta impedes the passage of the head or so obscures the upper pole that it cannot be grasped easily If further attempts at version are to be made, it is clearly of value to know on which side the placenta lies, so that it can be avoided It is even more important to exclude o presence of placenta prævia (unusual though it is th a breech) before making further attempts, especially anæsthesia is contemplated

) *Cases due for surgical induction in which the presenting rt is unengaged*

A not uncommon type of case is that in which there toxæmia necessitating induction but the head is not gaged though it can be pushed in In such circumstances acenta prævia can often be excluded clinically but it is ll possible for a placenta on the posterior wall to extend w enough to be disturbed by a Drew Smythe catheter bviously, it would be valuable to know that the placenta elsewhere and out of range (only then, indeed should a Drew Smythe catheter be used) Bender s figures 953) relating to the cause of bleeding in placenta prævia aphasise the danger of using this instrument in unsuitle cases

) *Other indications*

(a) *Previous classical cæsarean section* —Since rupture the uterus is thought to be more common if the acenta is implanted on the uterine scar it is as well to low the placental location in the latter weeks so that e risk may be lessened by admitting the patient to spital before term

(b) *Situation of placenta when it is prævia.*—When acenta prævia has been diagnosed by placentography e actual extent of the placenta on the anterior wall is own before operation and the technique can be anned so as to minimise maternal and fœtal blood loss. acentography may also be considered a useful prelimin y when cæsarean section is to be done under local algesia

(c) *Antepartum hæmorrhage especially before the 30th ek* —If placentography is done routinely a radiograph the fœtal skeleton is automatically available Gross ngenital abnormalities (which are more common when e placenta is prævia) may be seen and useless con rvative management for the sake of the fœtus thereby oided

Results

PLACENTA PRÆVIA

Of 50 cases of placenta prævia (table I) 1 was missed, ving a 2% error for placenta prævia The mistake was ade early in the series and was due entirely to inex rience in interpretation Nothing similar has happened since and in cases of significant placenta prævia in the last 6 weeks of pregnancy the error should be nil Where the diagnosis is on the borderline this should be made clear in the radiological report Such cases are found mostly when placentography is undertaken too early in the last trimester, before the lower segment has become well formed In a few cases the condition is truly border line—that is to say, the head is displaced only a little from the symphysis or promontory when the placenta extends down the anterior or posterior wall The level of the upper boundary of the lower segment is undoubtedly variable but in this technique it is assumed always to be at the pelvic brim The vagueness of this important landmark makes it all the more desirable for radiologist and obstetrician alike to be guarded in the special circumstances already mentioned before stating categorically that the placenta does not reach into the lower segment, and to be prepared to make a diagnosis of ' borderline placenta prævia

ABLE I—FEATURES OF 50 CASES OF PROVED PLACENTA PRÆVIA

marks on diagnosis :			
Correct	46		
Erroneous	1		
Borderline	3		
se confirmed			
Cæsarean section	31		
Postpartum intra uterine palpation	7		
Postpartum inspection	8		
Examination under anæsthesia	10		
Some cases were confirmed by more than one method			
nical features :	No of cases	Earliest diagnosed	Latest diagnosed
Antepartum hæmorrhage alone	23	30th week	40th week
A P H. plus high head &c	13	26th week	41st week
High head &c malpresentation	14*	32nd week	40th week
(Of these 14 cases diagnosed bef re bleeding took place 4 were of 4th degree ; 4 were discovered b fore the 30th week ; and 7 had no bleeding at any time 1 of these being of 4th degree.)			
Average birth weight	6 lb. 11 oz.		
tal and neonatal deaths	8 (16%)		
Prematurity	4		
Prolapsed cord	1		
Placental infarct (intra uterine death)	1		
Cord strangulation	1		
Atelectasis	1		

grees of placenta prævia and method of treatment

Degree	No. of cases	Average birth weight	Fœtal loss	Fœtal abnormalities	Cæsarean section	Version	Artificial rupture of membranes	Nil
1st	[illegible]	7 lb. 5 oz.	2	2	6	0	0	11
2nd	12	5 lb. 11 oz.	3	0	8	1	1	3
3rd	3	5 lb. 13 oz	1	0	3	0	0	0
4th	14	6 lb. 11 oz	2	0	14	0	0	0

There were no maternal deaths

In this series the radiological diagnosis of placenta prævia was in each instance confirmed or refuted before during or after delivery by examination under anæsthesia, cæsarean section or postpartum intra uterine palpation or by careful inspection of the placenta and membranes Neither of the last two methods is entirely satisfactory In the first place, owing to uterine retraction the placental edge either separated or still attached will often feel uncommonly low at the beginning of the third stage Where possible these findings should therefore, always be confirmed by inspection of the placenta and membranes after delivery Secondly the inspection of the placenta and membranes as a means of confirming the placental level will only be of value when the hole in the membranes has not been grossly enlarged and when the gestation sac has been expelled intact Again after measuring the distance between the placental edge and that of the hole doubt often remains as to whether the placenta did in fact reach the lower segment Where the hole was of average dimensions a distance of less than 2 in immediately placed the case in the category of placenta prævia We therefore conclude that if the diagnosis is not made before delivery in doubtful cases, the doubt will seldom be removed by any postpartum method of examination including that of injecting the placenta via the umbilical cord with radio-opaque substances (Radio-opaque substances were not used in this series for the method was regarded as having no special merit) Finally even by examining a patient under anæsthesia before delivery it would not always be possible to feel the edge of a placenta that just reached into the lower segment, especially when the cervix is not well drawn up and when the placenta is posterior

Clinical Features

The largest group is that of antepartum hæmorrhage alone because the bleeding most commonly began before the fœtus was big enough to be regarded as unstable or unduly high The earliest diagnosis was made at 30 weeks yet strangely enough an even earlier one (at 26 weeks) was made in the next group of antepartum hæmorrhage and high head &c It might be argued that this pregnancy was not far enough advanced for the presentation to be significant yet in central placenta prævia (as this one was) the fœtus will often be found unduly high even at a comparatively early stage The difficulty of trying to rely on abdominal palpation alone to diagnose placenta prævia even when there is both antepartum hæmorrhage and a high presenting part is well shown by comparing the number of cases of antepartum hæmorrhage and high head in table I with that in table II In the placenta prævia series only 13 out of 50 (or just over a quarter) fell into the antepartum hæmorrhage and high head ' group whereas in the other cases there were 25 out of 84 (or slightly less than a third)—figures which are distinctly comparable.

Placenta prævia was diagnosed before any bleeding took place in 14 out of 50 cases (or nearly a third), these having been radiographed purely because of the abnormal relationship between the presenting part and the pelvic brim This suspicious sign was acted on with positive findings as early as the 32nd week in 1 instance (and there were 3 others before the 36th week), and as late as the 40th week in another In 7 patients antepartum hæmorrhage was avoided entirely, even though the average maturity at diagnosis in these patients was 35 weeks, and 1 had a 4th-degree placenta prævia No fœtus was lost, and their average birth-weight was 6 lb 11 oz

Accidental Hæmorrhage

Although pre eclamptic toxæmia was found to accompany placenta prævia on 2 occasions, there was no evidence that the bleeding was accidental In fact 1 of these patients had no bleeding at all she had a 4th-degree placenta prævia and was delivered at term (by cæsarean section) of a thriving 8 lb 3 oz baby

Examination under Anæsthesia

This was carried out on 10 patients in whom placenta prævia had been diagnosed radiographically It was done for two reasons (1) to check the radiological findings early in the series (later it was used only in borderline cases), and (2) in the lesser degree of placenta prævia, especially anterior ones, to decide on the best method of treatment Disproportion due to posterior placenta prævia is a definite indication for cæsarean section, as was emphasised by Stalworthy (1951)

Fœtal Abnormalities

The incidence of fœtal abnormalities is known to be raised in placenta prævia Macafee's (1945) figure was 3 4% In this series two developmental abnormalities were found (a hare-lip, and a meningocele) In both cases the placenta prævia was of first degree

Average Birth-weight

The conservative management of antepartum hæmorrhage, particularly when it is due to placenta prævia, is now so well established as to require no further com mendation here The average birth-weight of 6 lb 11 oz in our 50 cases of placenta prævia is ample proof of the wisdom of such a policy

Fœtal and Neonatal Deaths

One of the aims in the modern management of placenta prævia is to reduce fœtal and infant loss without adding extra risk to the mother The mortality-rate of 16% in this series compares favourably with that in other reported series The average birth-weight of the fœtuses and infants lost was 5 lb 5 died after birth, the only abnormal finding being prematurity 3 were stillborn—1 from prolapse of the cord, 1 macerated from placental infarction, and 1 from the cord being tightly round the neck Table I shows that the loss was fairly evenly divided between the different degrees of placenta prævia It is unfortunate that 3 of the neonatal deaths followed cæsarean section In 6 of the patients concerned, active measures had to be undertaken to combat recurrent severe bleeding

Treatment

There were 31 cæsarean sections 14 were for 4th-degree and 3 for 3rd-degree placenta prævia Of the 8 done for 2nd degree, 1 was for a breech in an elderly primigravida, 3 were for posterior placenta prævia with apparent disproportion, and 4 were for excessive bleeding after artificial rupture of the membranes had failed to stop it In the other 2nd degree cases, bipolar version was done once when artificial rupture of the membranes did not stop the bleeding, simple artificial rupture of the membranes was also done, and in the remaining 3 cases no treatment was required 6 cæsarean sections were done for 1st-degree placenta prævia—2 for excessive bleeding, 2 for unstable presentation, 1 for associated diabetes mellitus, and 1 for prolapse of the cord

Maternal Deaths

There were no maternal deaths associated with pla prævia

Incorrectly Diagnosed and Borderline Cases

Case 1 —A para 5 with antepartum hæmorrhage, and fœtal head at 34 weeks Placentography showed a post placenta , the head was displaced significantly, but thi erroneously thought to be due possibly to clot B continued, and examination under anæsthesia showe marginal placenta prævia Artificial rupture of the mem and bipolar version stopped the bleeding, but an imm infant of 4 lb 3 oz was delivered, which died after hours This case was one of the earliest in the series Th mistake was not in technique but in interpretation, and w due entirely to inexperience

Case 2 —A para 2 with antepartum hæmorrhage at weeks Placentography revealed no significant displacem of the head, and it was reported as showing "no evidence placenta prævia " The patient subsequently had a norm labour with no further bleeding, but postnatal inspection the placenta suggested that it was low lying—possibly degree The infant weighed 6 lb 1 oz and did well.

Case 3 —A primigravida with a high head at term. Pla tography showed an anterior placenta and no significant placement *Normal delivery took place with no bleeding*, there was a 40 oz postpartum hæmorrhage Postpa intra-uterine examination suggested that the placenta just reach into the lower segment anteriorly and was po a 1st-degree placenta prævia The infant weighed 10 lb. and did well

Case 4 —A primigravida with antepartum hæmorrhage a high head at 35 weeks Placentography showed a post placenta and there appeared to be no significant displace from the promontory to suggest that the placenta reached *the lower segment The patient was examined* under thesia, and a thin edge was thought to be felt high up teriorly A 5 lb 9 oz infant was delivered spontaneous and it did well. There was no report of a postpartum inspe of the placenta and membranes to confirm this case

TABLE II—FEATURES OF 84 CASES IN WHICH ANTEPART HÆMORRHAGE WAS NOT ASCRIBED TO PLACENTA PRÆV

Remarks on diagnosis
  Placenta prævia correctly excluded
  Placenta prævia erroneously diagnosed
  Borderline

How confirmed
  Cæsarean section
  Postpartum intra uterine palpation
  Postpartum inspection
  Examination under anæsthesia

Factors associated with antepartum hæmorrhage
  Pre-eclamptic toxæmia
  Benign hypertension
  External cephalic version
  Erosion
  Cervical polyp
  Short umbilical cord
  Unknown

Average *time in hospital* before 36th week = 11 days
Reckoned average *time saved* before 36th week = 8 days

Placental site in 65 cases of unexplained antepartum hæmorrhage
  Posterior and fundal
  Anterior
  Cornual
  Lateral

Clinical features	*No of cases*	*Earliest diagnosed*	*Lat dia*
Antepartum hæmorrhage alone	59	26th week	41st
Antepartum hæmorrhage, plus high head &c	25	32nd week	40th
Average birth weight			6 lb 7 lb

Fœtal and neonatal deaths
  Associated factors
    External cephalic version
    Benign hypertension
    Postmaturity 6 weeks
    Prematurity
    Asphyxia

Treatment	*No of cases*	*Stillbirths and neonatal d*
Normal labour	58	3
Twin labour	1	[illegible]
Breech labour	5	1
Medical induction	2	0
Surgical induction	6	0
Forceps	6	1
Examination under anæsthesia	2	0
Cæsarean section	3	0

There was 1 maternal death (due to ovarian carcinoma).

BLE III—FEATURES OF 113 CASES WITH HIGH HEAD BREECH NSTABLE PRESENTATION &C. (NO ANTEPARTUM HÆMOR HAGE AT THE TIME OF DIAGNOSIS)

ification of placenta	
rrect	109
correct	1
orderline	3
confirmed :	
xamination under anæsthesia	3
stpartum intra-uterine palpation	16
stpartum inspection	8
rgical induction	4
sarean section	27

ociated factors :	*High head*	*Breech*	*Unstable presentation*	*Total*
acenta prævia	6	3	6	14
ontracted pelvis	8	0	1	9
elvic tumour	6	1	0	7
ultiple pregnancy	0	0	0	0
ornual implantation	0	*4 (+1)	0	*4
ydramnios	0	0	1	1
nknown	40	8	10	58

ental position in 35 breech cases			
nterior wall	5	Lateral wall	0
osterior wall	0	Anterior and fundal	2
undal	0	Posterior and fundal	1
ower segment	2	Cornual	25

The only serious error in these so-called missed “ cases, ’ s made in case 1 and was due to inexperience in terpretation None of the other 3 behaved subsequently e placenta prævia cases and if in fact they were y were not of significant degree and would be correctly sed as borderline only No fœtus or mother suffered a result of the error for although the baby in case 1 d, the negative radiographic findings encouraged the tinuation of conservative treatment to avoid pre turity It was further bleeding that caused the birth a fragile premature infant

ANTEPARTUM HÆMORRHAGE NOT DUE TO PLACENTA PRÆVIA

There were 84 cases of antepartum hæmorrhage not e to placenta prævia (table II) In 82 a correct diagnosis s made by radiography leaving 2 cases incorrectly gnosed 1 was a borderline case at the 39th week, d little time was wasted by the patient in hospital. e other, unfortunately spent four weeks in hospital necessarily, through an error due to inexperience in chnique Of these 84 cases the absence of placenta ævia was confirmed in 45 (table II) All the other cases haved quite normally and gave no indication of low plantation

use of Antepartum Hæmorrhage

In only 3 patients were there signs of toxæmia, and in ch instance examination of the placenta after delivery ongly supported a diagnosis of toxæmic accidental morrhage It is significant that the commonest sociation was with external cephalic version The use of the bleeding was not found in 65 of the patients

ition of the Placenta in the Upper Segment

It was thought that non toxæmic antepartum hæmor age might be associated with the position of the placen l site A likely position would seem to be the anterior erine wall reaching nearly to the pelvic brim ; there e placental site would be vulnerable to trauma and be ar enough to the cervix for the blood to escape readily ble III shows that the commonest site for the placenta non toxæmic antepartum hæmorrhage is, in fact the terior wall extending to the fundus the anterior all is the next commonest

ditional Clinical Signs

As might be expected bleeding was the only abnor al feature in over two-thirds of the cases We have ready drawn attention to how often bleeding and lative displacement of the presenting part can be found ether in the absence of placenta prævia Much portance is attached to this observation for dangerous complacency or over anxious conservatism may result if the precision and safety of soft-tissue radiography is denied both to patient and clinician

Average Stay in Hospital

If by staying in hospital a patient is doing good for herself and for her fœtus, then it would be wrong to suggest that she go home But there is no evidence that in the absence of other symptoms and signs, there is any advantage in keeping patients in hospital once placenta prævia has been excluded and once bleeding, which is usually slight, has stopped This belief determined our policy in this series. Even so, the average stay in hospital before the 36th week was reached proved to be as much as 11 days this relatively high figure is largely explained by our having to keep in patients who bled too early for placenta prævia to be excluded radiographically Even though in 1 instance placenta prævia was excluded correctly at the 26th week it is unusual to be able to give a positive diagnosis before the 34th The arbitrary time of the 36th week was decided on because those who diagnose placenta prævia by passing a finger through the cervix under anæsthesia usually wait until then to do so

Reckoned Average Time Saved

The saving of 8 days in hospital seems small enough, but with many patients the bed saving is considerable Those who doubt the value of soft tissue placentography say that this aspect of the management should be discounted ; but it is of real and practical importance both to these patients and to those who are waiting to occupy the beds.

Average Birth-weight

This was 6 lb 6 oz —lower than the reported average for placenta prævia

Fœtal and Neonatal Deaths

7 fœtuses and infants were lost giving a figure of 8 3%—about half that for placenta prævia 1 at least of these cases could hardly have had any connection with antepartum hæmorrhage the fœtus, said to have been 6 weeks postmature and weighing 11 lb died during and as a result of a very difficult delivery The other deaths cannot be attributed to our policy of discharging patients who had bled but in whom placenta prævia had been excluded radiographically since all the patients concerned were kept in hospital from the time of bleeding until they were delivered.

Fœtal Abnormality

No developmental abnormality was found in any fœtus in this group

Maternal Death

The only mother lost died some 2 months after delivery from ovarian carcinoma with pulmonary metastases

Incorrectly Diagnosed and Borderline Cases

Case 5 —An elderly primigravida with persistent breech presentation at the 34th week and a little bleeding after an attempt at version had failed. Placentography suggested posterior placenta prævia of significant degree but subsequent cæsarean section at term for the presentation revealed an anterior placenta in the upper segment This was again very early in our series and before we began to use the tilted lateral view in doubtful cases. A healthy 7 lb 10 oz. baby was delivered. (Eighteen months later significant posterior placenta prævia was again diagnosed in this patient s second pregnancy at the 34th week, breech again presenting This time the tilted lateral view was taken and subsequent cæsarean section proved the diagnosis correct)

Case 6 —A para-5 with antepartum hæmorrhage and an unengaged head at the 39th week. The placentographic films were poor in quality and a full view of the uterus was not available A borderline posterior placenta prævia was diagnosed. Examination under anæsthesia was done but no placenta was felt (No postpartum examination or inspection of the placenta and membranes was recorded to confirm this finding) A healthy 7 lb 13 oz infant was subsequently delivered

HIGH HEAD, BREECH, OR UNSTABLE PRESENTATION, &c

The primary indication for placentography in this group (table III) was either an unduly high presenting part, or an unstable presentation suggesting the possibility of a low-lying placenta, in the absence of any other detectable cause Mostly the patients had reached the last month of pregnancy, but in some placenta prævia was suspected well before the 36th week, solely on the relationship of the presenting part to the brim As table I shows, 1 case of placenta prævia was suspected and proved by radiography as early as the 32nd week The patients who had a pelvic tumour were radiographed both to test the technique in these circumstances and to exclude the co-existence of placenta prævia Of 113 cases, radiographic localisation of the placenta was correct in 109 In only 1 case was the diagnosis said to be incorrect

Case 7 —A para 3 with an unstable presentation at 36 weeks Posterior placenta prævia was diagnosed by placentography, but near term the fit of the head threw doubt on the diagnosis, so artificial rupture of the membranes was done to stabilise the presentation When labour began, bleeding was so severe that cæsarean section was undertaken. The surgeon, however, was of the opinion that the placenta did not reach the lower segment No cause for the bleeding was suggested, and we offer no other explanation There were no signs of toxæmia, and a healthy 7 lb 2 oz infant was born

The other 3 cases were essentially borderline 1 of them, case 3, has already been discussed

Case 8 —A para 2 with a very unstable presentation at 35 weeks Placentography was reported as showing a minor degree of posterior placenta prævia There was no antepartum hæmorrhage or any departure from normal in the subsequent labour at term, when a healthy 6 lb 8 oz infant was delivered No postpartum intra uterine or placental examination was recorded This, therefore, must rank as an error in diagnosis, *although it is possible that such a minor amount of placenta* dipping below the brim might either have been carried up later by uterine growth, or been so slight as to cause no trouble

Case 9 —A *primigravida* with a high head at 39 weeks Placentography suggested a minor degree of posterior placenta prævia, because of slight forward displacement of the head and the placenta occupying the posterior wall No bleeding took place during labour, which began at term, but the head engaged slowly Delivery was uneventful Unfortunately there is no record of examination after labour

No mother or fœtus was lost as a result of these debatable errors No gross mistake was made in missing significant placenta prævia The errors, as they should be in this work, were rather those of commission than omission When there is doubt, "placenta prævia" should be diagnosed Just over half of the cases were confirmed by one or other of the usual methods In the remainder there was no departure from normal to suggest a low-lying placenta The different reasons for the ill-fitting or abnormal presenting part are shown in table III In about half no cause was found This is too high a proportion and simply means that such common conditions as multiparity, occipitoposterior, pelvic inclination, and hydramnios have not been recorded in the notes

Table III also shows the comparative rarity of breech presentation in placenta prævia or contracted pelvis and pelvic tumour on the one hand, and the significant coincidence of cornual implantation and breech presentation on the other Of the 35 cases of breech presentation investigated, the placenta occupied the cornual position in no less than 24 In our series, as in Stevenson's (1951), this position was the commonest finding associated with breech presentation, and it is the most probable cause of persistent breech presentation The placental position in the [illegible] cases is shown in table III In 1 case there was both pelvic tumour and cornual implantat but precedence has been given to the tumour as the c of the breech

Further Points

Transverse or Oblique Lie

The very essence of soft tissue placentography is t use the contrasting outline of the fœtus to show by displacement the position of the placenta Unless lie is axial, with the lower pole over the brim, the imp tant brim area cannot be examined accurately, and the obstetrician should be present in the X ray depart to correct the lie immediately before placentography

Pelvic Tumour and High Head

Obviously the diagnosis of pelvic tumour will be ma by clinical examination, but it is not by any means e to exclude the co existence of placenta prævia clinical Even when the radiologist knows of the presence of pelvic tumour, if the placenta extends well down th posterior wall it is not always possible to be sure that of the head displacement is not due partly to place prævia The same is true when the head is displaced a rectum grossly distended by fæces The difficulty d not arise when the placenta is on the anterior wall fundus, for the radiologist can then diagnose the of the displacement with confidence In practice, fr the aspect of delivery, it is of no importance to disting between tumour and placenta prævia, because cæsar section will be needed in both However, for safe an natal management it is important to know of possibility of placenta prævia

Early Diagnosis

Before about the 34th week precise diagnosis can made only when the placenta is implanted mainly are the fundus, or mainly in the lower segment Even wh the placenta appears to extend from the anterior posterior walls into the pelvis, at this early stage it impossible to predict how much will remain there as th uterus grows and the lower segment forms Natura if a case is borderline so early it will almost certa become negative for placenta prævia at a later date wh further placentography should be done A correct dia nosis was made in 5 of our patients by the 30th wee In 3 placenta prævia was excluded, in 2 major place prævia was discovered, and both subsequently need cæsarean section

Placenta Prævia and the Presenting Part

The relationship of the presenting part with the pe brim is used both clinically and radiologically to dia placenta prævia, and the more experienced a clini becomes the closer will he approach the precision placentography, yet it is only in the more extre forms of placenta prævia that he is likely to achieve comparable degree of success Similarly, it is only wh the presenting part is deeply engaged and can be palpa readily through the fornices that placenta prævia ca be excluded as the cause of bleeding in a particu patient In between these extreme examples are fou the majority of cases of antepartum hæmorrhage, a clinically there must be doubt about the position of th placenta Even when the head can be engaged read at term there can still be significant placenta præv The following case is an example of this

Case 10 —A para 1 had a little vaginal bleeding at ter The head was resting in the brim and could be eng readily The placentography report stated there was signific displacement compatible with the presence of posterior plac prævia Cæsarean section was done and a posterior mar placenta prævia was found

Radiological Technique

The technique used was essentially that described b Reid (1949) and by Whitehead (1953), but we reduc the number of films taken to two—an anteroposterio standing lateral which included the whole of the s and the pelvic inlet In some a third view was d—the tilted lateral where the standing lateral s apparent forward displacement Very occasionally views may be required in cases of hydramnios

gh kilo voltage (115–120 kV) is used for lateral . Development is cut to 3½ min to avoid over ening of the part of the film which shows the ior wall

o patient must empty the bladder immediately e examination If the rectum is too full of fæces procedure may have to be repeated.

Summary

lt tissue placentography is a practical method of ting the placental site The margin of error is iderably less than with clinical methods.

advantages are greatest in the conservative manage t of antepartum hæmorrhage

cases of major degree placenta prævia the hazards gital exploration of the lower segment can be avoided gether Only in lesser degree or borderline placenta ria, in which the risk of severe bleeding is propor ately less, may examination under anæsthesia be led, either for final diagnosis or treatment.

he method has proved particularly useful in patients ected of having placenta prævia before they have l.

hat certain placental positions may cause persistent ech presentation has been confirmed by our observa s No association was found between the placental and accidental antepartum hæmorrhage

REFERENCES

der S. (1953) *J Obstet Gynæc. Brit Emp* 60 508
aler C. G H (1945) *Ibid*, 52 313
r J. C. (1944) *Amer J Obstet Gynec* 47 198
d, F (1949) *Brit J Radiol* 22 557
w W., Powell C. B (1934) *Amer J Roentgenol* 31 37
worthy J (1951) *Amer J Obstet Gynec* 61 720
renson, C B (1951) *Ibid* 62 486
itehead A. S (1953) *Brit J Radiol.* 26 401

TREATMENT OF ADRENOGENITAL SYNDROME

WITH CORTISONE AND ŒSTROGEN

C N ARMSTRONG
M.D Durh F.R C.P D.P.H
PHYSICIAN ROYAL VICTORIA INFIRMARY
NEWCASTLE UPON TYNE

In cases of adrenogenital syndrome presenting female udohermaphroditism due to hyperplasia of the adrenal nds, continuous treatment with cortisone reduces the ical masculine features and the urinary excretion 17 ketosteroids and promotes the development of inine characteristics (Wilkins et al 1950 1951 1952, Vines and Dods 1954) To obtain this result large doses of cortisone (100–200 mg daily by mouth) may have to be given, and this presents difficulties where supplies of cortisone are restricted

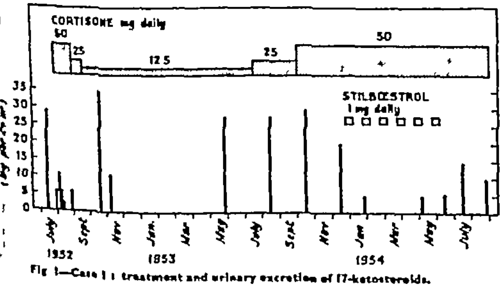


Fig 1—Case 1 : treatment and urinary excretion of 17-ketosteroids.

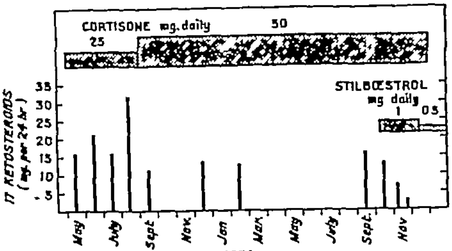


Fig. 2—Case 2 : treatment and urinary excretion of 17-ketosteroids

Treatment of such cases with œstrogen alone produces neither clinical improvement nor reduction in the excretion of 17 ketosteroids. In the following three cases, however combined therapy with œstrogen and cortisone was successful.

Case 1 —*A girl aged 10 years, was admitted to the Royal* Victoria Infirmary Newcastle upon Tyne with male body contours, severe hirsutism pubic hair of male distribution, undeveloped *breasts, and urinary excretion* of 17 ketosteroids 36 mg per 24 hours A congenitally large clitoris had been amputated

Laparotomy revealed uterus vagina, and ovaries Right adrenalectomy was performed but produced no improvement

Treatment with oral cortisone was begun with 50 mg daily in 1952, when the patient was 16 and the urinary excretion of 17 ketosteroids was reduced from 29·0 mg to 2 8 mg The dosage of cortisone was reduced to 25 mg and later 10 mg daily with no change in the clinical picture The excretion of 17 ketosteroids increased to 30 mg ; so *the cortisone dosage was increased to 50 mg daily* When the excretion of 17 ketosteroids was 21 mg under this dosage of cortisone I prescribed (for acne) 1 mg of stilbœstrol *daily for 14 days followed by 14 days without stilbœstrol,* the dosage of cortisone remaining 50 mg daily The excretion of 17 ketosteroids decreased rapidly to 4 5 mg in 24 hours I increased the dosage of stilbœstrol to 2 mg daily and then stopped it whereupon the urinary excretion of 17 ketosteroids immediately began to increase (fig 1) Coincident with the decrease in excretion of 17 ketosteroids there was clinical improvement

Case 2 —*A girl aged 9 was admitted to the Royal Victoria* Infirmary with a deep voice a hypertrophied clitoris, well developed pubic hair; the vagina was present Urinary excretion of *17 ketosteroids* 23 6 mg per 24 hours Left adrenalectomy did not produce any clinical improvement

Treatment with cortisone was started when the patient was aged 12 and her excretion of 17 ketosteroids was 10 mg per 24 hours. The dosage was 25 mg daily and was later increased to 50 mg daily The excretion of 17 ketosteroids fluctuated somewhat but the smallest amount excreted was 11 mg in 24 hours and the girl's breasts began to develop when the excretion of 17 ketosteroids was 15 3 mg Stilbœstrol 1 mg daily was prescribed in addition to the 50 mg of cortisone daily and the excretion of 17 ketosteroids decreased to 6·8 mg and later 2 3 mg per *24 hours (fig 2) Menstruation was also* established.

Case 3 —In this girl an enlarged clitoris was found at the age of 1 year and pubic hair began to grow at the age of 2½ years In 1953 when she was aged 14 treatment was started with oral cortisone 50 mg daily The excretion of 17 ketosteroids decreased from 23 0 mg per 24 hours to 12 2 mg *and later* to 7 8 mg but increased again to 10·5 mg The breasts began to develop and menstruation

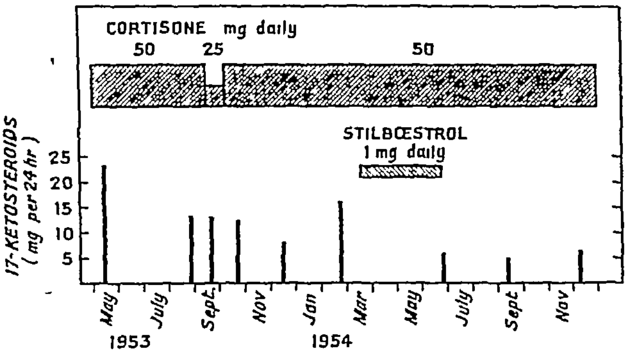


Fig 3—Case 3 : treatment and urinary excretion of 17-ketosteroids

was established With the dosage of cortisone kept at 50 mg daily stilbœstrol 1 mg daily was prescribed, and the urinary excretion of 17 ketosteroids decreased to 6 0 mg per 24 hours (fig 3) Stilbœstrol therapy had to be stopped then because of heavy menstrual bleeding

These cases show that, in the treatment of female pseudohermaphroditism, administration of œstrogen and cortisone is more effective than cortisone alone in reducing a high urinary excretion of 17-ketosteroids

REFERENCES

Vines, R , Dods L (1954) *Aust Ann Med* 3 5
Wilkins, L , Gardner, L I , Crigler J F et al (1952) *J clin Endocrin* 12, 257
— Lewis R A Klein, R , Rosemberg, E (1950) *Bull Johns Hopk Hosp* 86, 249
— — — Gardner L I , Crigler J F , Rosemberg, E , Migeon C J (1951) *J clin Endocrin* 11, 1

MASSIVE BLOOD-TRANSFUSION THROUGH THE CEPHALIC VEIN

E G Dolton
M B Lond , F R C S
THORACIC SURGEON, ROYAL HOSPITAL, WOLVERHAMPTON

Patients undergoing major thoracic surgery may need very rapid transfusion of considerable quantities of blood Cannulation of the internal saphenous vein at the ankle leads to a disappointingly slow flow In the commonly favoured lateral position this may be partly due to compression of the saphenous vein at the knee and in the thigh by the opposing limb or an intervening pillow, and also possibly the opened chest and relaxed abdominal muscles lessen the negative pressure responsible for normal systemic venous flow Needling of an arm vein is more effective but often unsatisfactory Intra-arterial transfusion gives a rapid replacement of blood lost by major cardiac or vascular injury but is not easy to do, requires a special pump and expert medical and leads to an excess of potassium in the (Melrose and Wilson 1953)

of cephalic vein in intermuscular groove.

What is wanted is a large cannula inserted into a superficial vein reasonably near the heart No the inferior vena cava is of use, but the external vein and the cephalic vein near the shoulder satisfy criteria Use of the external jugular would lead to a on the neck , therefore the cephalic vein is to be I was encouraged to use this vein by Dr N H then casualty registrar to this hospital, who told had given infusions through the cephalic vein successfully in cases of burns

My assistants and I have cannulated the cephalic in over 100 cases, in the past twelve months. The runs very freely, venospasm has not occurred, and pint of blood can be completely transfused within minutes without any form of pressure The vein is *thin-walled, easily dilated at the site of* tion, and admits an unexpectedly large cannula ease This method has proved eminently satisfactory without any complication, and I recommend it to engaged in major surgery and not blessed with assistants

The only disadvantage has been that on nine the cephalic vein has been absent from its normal tion Such patients have had *small transverse* taneous veins across the front of the shoulder, and I not now explore for the cephalic vein when such veins present

Anatomy

The cephalic vein begins on the radial side of dorsum of the hand, runs up the radial side of the and at the bend of the elbow gives off a median branch medially to join the basilic vein Thereafter travels up the outer side of the arm lateral to the muscle until it crosses the anterior aspect of the of the deltoid muscle , it next approaches from lateral side the groove between the deltoid muscle the pectoralis major muscle, *and soon runs* in the itself (see figure) , about two inches higher the sinks deeply into the groove and becomes difficult to by ordinary dissection No artery accompanies it ever deepening course leads it to the fascia, which it pierces, and it ends in the vein The junction of tributary with recipient vein be guarded by valves, but these are often absent

This description is based *on surgical* exploration on several post-mortem dissections

Procedure

It has been found convenient to cannulate the when general anæsthesia has been induced and with patient supine The arm which will be uppermost operation is selected, because flexion and the *lowermost arm* has caused angulation of the and failure of the drip With the arm held away from side of the body at about 45° (most easily by placing the hand under the upper part of the an incision 2 inches long along the lower part of deltoideopectoral groove, and extending just below beginning of that groove, will expose the vein If vein is not in the groove it will be found slightly laterally, over the deltoid muscle The vein is thin easily dilated, and in an adult takes the largest Bailey cannula , the medium Bailey cannula and normal adult *Sutton cannula* can usually be into the vein of a child aged 5–10 years After I customarily insert a distal skin stitch which cannula in its second loop, and a proximal skin which, passing under the vein, is left long and until after the cannula has finally been removed

REFERENCE

Melrose, D G , Wilson, A O (1953) *Lancet*, i, 1266

THROMBOCYTOPENIC PURPURA SSOCIATED WITH OXYTETRACYCLINE THERAPY

A G BECKETT
B.M Oxfd M R C.P
NIOR MEDICAL REGISTRAR, ROYAL FREE HOSPITAL, LONDON

A. W H. FOXELL
M.B Lond
EMATOLOGIST, NORTH WESTERN GROUP LABORATORY LONDON

ALTHOUGH oxytetracycline is known occasionally to use toxic reactions in the skin and gastro intestinal act, no case of blood dyscrasia (including thrombo topenic purpura) due to this drug has been reported in is country

In a nation wide survey of 1448 cases of blood dyscrasia the United States, Welch et al (1954) report 41 cases of blood orders associated with oxytetracycline therapy including cases of thrombocytopenia in 4 of which no other drug s given. The outcome and details of these cases are not ported. Of the 499 cases of thrombocytopenia 62 were ssified as due to 'infection' and 266 as idiopathic. It is refore possible that some or all of the cases associated with ytetracycline therapy should have been classified under ther of these headings.

We describe here a case of thrombocytopenic purpura ssibly due to oxytetracycline

Case-report

A man, aged 77 was admitted to hospital on Oct 19 1954 th bilateral pneumonia, which had started 10 days earlier th tiredness followed 3 days later by pain in the chest and termittent ache in the right ear For at least 10 years he had d Paget's disease of bone 8 years previously he was found have diabetes mellitus, which was subsequently treated by et alone. There was no history of any tendency to morrhage.

On admission his temperature was 99°F pulse rate 100 d respirations 28 per min. He was flushed and dyspnoeic th signs of consolidation at the left base and coarse crepita ons with expiratory rhonchi at the right base He had a llapsing pulse and blood pressure 160/70 mm. Hg Paget's sease of the tibiæ was present the changes being more onounced in the right leg There was no retinopathy the ee and ankle jerks were absent but vibration sense was esent.

vestigations

Radiography of the chest showed extensive pneumonic anges in the lower zones, greater on the right side On ct 20 the hæmoglobin was 90% (13·3 g per 100 ml) and the hite cells were 9000 per c.mm. (differential count of normal stribution); the erythrocyte-sedimentation rate (E.S.R.) as 120 mm. in 1 hour (Westergren) The serum alkaline osphatase level was 9·5 King Armstrong units per 100 ml he sputum contained scanty pus cells and on culture grew *reptococcus viridans* Cultures of swabs from ear and eye ere sterile

reatment and Progress

Treatment with penicillin and sulphadiazine started on the ening of admission by his private doctor was continued r 24 hours; but, as there was no improvement and his ndition was serious, these drugs were stopped and he was ven a course of oxytetracycline 1·0 g initially followed by 5 g. twice daily Little or no improvement followed at first cute otitis media was diagnosed on Oct 24 and was treated ith chloramphenicol in propylene glycol which was applied to e auditory meatus on a wool wick 6 hourly for 18 hours. yringotomy was then performed under general anæsthesia nd the discharge stopped a few days later

On Oct. 26 the patient had acute cardiac failure which proved after venesection and administration of oxygen and travenous aminophylline Subsequently he was treated ith digitalis and mersalyl and had no further episodes. ecause of the severity of the illness and this episode of rdiac failure the dosage of oxytetracycline was increased ·5 g 6 hourly being given for the next 6 days. This produced clinical improvement the symptoms decreasing and the temperature, which had been 99–100°F falling to normal The signs in the lungs did not change however and radiography showed increased shadows in both lower zones extending into the mid zone on the left

The white-cell count, which on Oct 27 was 21 000 per c.mm (neutrophils 91%) fell to 10 000 per c.mm. 9 days later The E.S.R. was now 65 mm. in the first hour The sputum again produced a heavy growth of *Strep viridans* Oxytetracycline was continued on a reduced dosage 1 g daily in two divided doses for 8 days, making a total of 26 g in 22 days.

Blood Dyscrasia

On the third day after stopping the oxytetracycline the patient had a severe epistaxis followed next day by more epistaxes and gross hæmaturia By this time he had developed extensive hæmorrhagic purpura During the next 24 hours many fresh cutaneous hæmorrhages appeared and the hæmaturia continued At this stage he had normochromic and normocytic anæmia thought to be due to blood loss The hæmoglobin was 66% (9·8 g per 100 ml) red cells were 3 270 000 per c.mm and white cells 18,000 per c.mm. (neutrophils 63%); his platelets had decreased to 15 000 per c.mm The bleeding time was much prolonged no evidence of cessation of bleeding occurring after 18 minutes. The prothrombin time and clotting time were normal and the Hess test was positive Next day there were further skin hæmorrhages and hæmaturia. The hæmoglobin was 62% (9·2 g per 100 ml) platelets were 11 000 per c.mm. and white cells 16 700 In the evening he started to cough up bloodstained fluid and vomited coffee grounds. His general condition deteriorated rapidly and in the early hours of Nov 17 he died

The Sternal Marrow

Sternal marrow puncture was done 15 minutes after death the differential marrow count being as follows: myeloblasts 1% promyelocytes 1% neutrophil myelocytes 8% metamyelocytes 8·5% neutrophil polymorphs 51%, eosinophil polymorphs 1%, early normoblasts 4% intermediate normoblasts 6% late normoblasts 14·5% plasma cells 0·5% lymphocytes 4% and monocytes 0·5% The myeloid/erythroid ratio was 2·9/1 There was no evidence of platelet production, and only an occasional promegakaryocyte was present. No other evidence of toxic changes was seen. The development of the myeloid and erythroid series was normal apart from some increase in mature polymorphs.

Necropsy

There were numerous petechiæ in the skin of the trunk and limbs, the pericardium and endocardium, and the mucosa of the stomach small intestine colon and urinary bladder Ecchymoses were present in the pelves of the kidneys and in the leptomeninges over the left frontal and parietal lobes of the brain The lungs showed organising fibrinous pleurisy and gangrenous pneumonia with abscesses up to 2 cm. in diameter in the lower lobe of the left lung An older unresolved pneumonia, with abscesses up to 1 cm in diameter in the lower lobe of the right lung and œdema and congestion of the remainder of the lungs were also found The spleen showed subacute septic changes. Pus was present in the right middle ear The neck and upper half of the shaft of the right femur and the sternum contained red marrow

Discussion

Thrombocytopenia is occasionally associated with septicæmia but throughout his illness our patient did not show any clinical evidence of this and it seems improbable that the purpura was due to septicæmia He had suppurative pneumonia diabetes mellitus and Paget's disease of the bone none of which are known to produce thrombocytopenia

Sulphonamides and chloramphenicol cause thrombocytopenia on rare occasions, but we do not think they were responsible for it in this case because the sulphadiazine was given for only 24 hours to a total of 2·5 g and the bleeding did not come on until 3 weeks later Chloramphenicol was applied aurally only on three occasions in 18 hours and this local application could scarcely have had a toxic effect on the marrow

In spite of the widespread use of mercurial diuretics we have found only 3 published reports of thrombocytopenia possibly due to mercurials (Butt and Simonsen

1950) Similarly, although iodides have been extensively used for a long time, there are very few instances of thrombocytopenia due to iodides Dennig (1933) reported 2 unproven cases, and Davis and Saunders (1946) described a proven case of purpura, due to potassium iodide, in which the platelet-count on one occasion was 100,000 per c mm We think it most improbable that either mersalyl or elixir of caffeine iodide, both of which were given for a short time only, caused the thrombocytopenia in our patient In addition he was treated with aminophylline, digitalis, and chloral, none of which is known to cause thrombocytopenia Aspirin, amidopyrine, ‘Sedormid,’ and other drugs producing thrombocytopenia were not known to have been given either in hospital or in the previous 2 months

It therefore seems likely that the oxytetracycline was responsible for the thrombocytopenia in the present case The almost complete absence of any members of the megakaryocyte series seems to indicate that the action of oxytetracycline was to produce directly or indirectly a selective marrow depression affecting only the precursors of the platelets The only other toxic manifestations were those due to mild gastro-intestinal irritation, a complication not infrequently associated with the use of oxytetracycline

Although our patient's pneumonia appeared to have been held in check by the intensive drug therapy, the final outcome of his illness was determined by the thrombocytopenia this might have been reversible in a person less seriously ill

Summary

A case of thrombocytopenia purpura in a man, aged 77, with suppurative pneumonia is described The bone marrow showed selective depression of platelet production

The thrombocytopenia was possibly caused by oxytetracycline

We wish to thank Dr Una Ledingham for her permission to publish this case

REFERENCES

Butt, E M, Simonsen, D G (1950) *Amer J clin Path* 20 716
Davis W C, Saunders, T S (1946) *Arch Derm Syph Chicago*, 53 644
Dennig H (1933) *Münch med Wschr* 80 562
Welch, H, Lewis C N Kerlan I (1954) *Antibiot Chemother* 4, 607

Preliminary Communication

PITUITARY-RADON IMPLANT FOR BREAST CANCER

CERTAIN tumours, at some stage of their progression towards autonomy, may depend on hormones produced by the endocrine glands of their hosts For example, total ablation of the suprarenal glands and ovaries, by removing the sources of œstrogenic steroids, has proved of benefit in some cases of advanced mammary cancer The pituitary gland has also been removed for the same purpose,[1] but this major operation carries a significant mortality, so a method has been evolved at the Western Infirmary, Glasgow, of destroying the pituitary gland by implanting radon seeds, thus obviating the necessity for open operation

Technique

The seeds are introduced through a cannula inserted into the pituitary fossa through the nose and the sphenoidal sinus To enable this to be done under radiological control, an adjustable director apparatus, incorporating radio opaque protractors in two planes, has been constructed After the nose has been swabbed with spirit and a solution of 1 1000 adrenaline, the patient's head is fixed in the apparatus (fig 1), and the cannula is inserted through the director tube into the nostril Radiographs are taken in anteroposterior and lateral planes, and the alignment of the cannula is corrected accordingly The cannula is next advanced as far as the roof of the nose, and further radiographs are taken to confirm the alignment and to measure the distance from the point of the cannula to the sella turcica The trocar is inserted and by firm pressure the cannula is bored this distance through the sphenoidal air sinus and the base of the sella turcica The point of the cannula now lies within the pituitary fossa, this position being confirmed

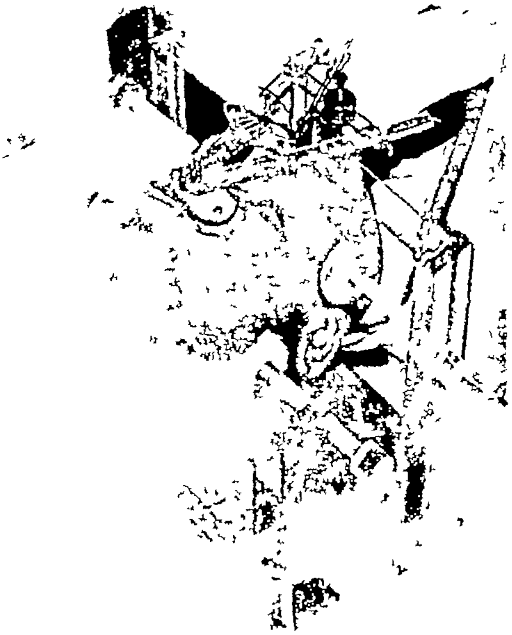


Fig 1—Head of patient fixed into apparatus and cannula into nostril

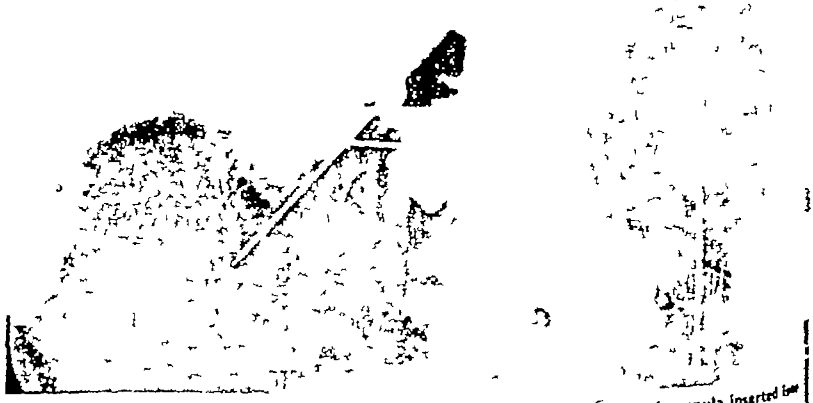


Fig 2—Anteroposterior and lateral radiographs of skull, showing trocar and cannula inserted in pituitary fossa.

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[1] Luft, R Olivecrona, H *J Neurosurg* 1953, 10 301

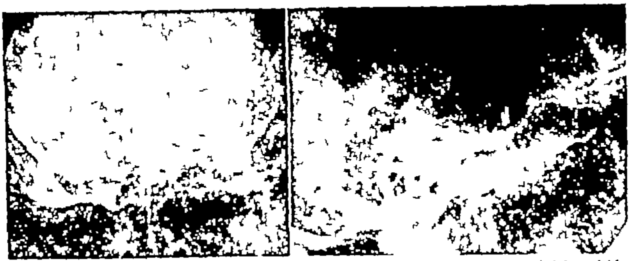

Fig 3—Anteroposterior and lateral radiographs of pituitary fossa showing two seeds lying within gland.

her radiographs (fig 2) Radon ds are introduced (fig 3) the rument is withdrawn and the al cavity is packed with gauze ked in adrenaline solution is pack is removed after twelve urs

Results

This operation is done under neral anæsthesia and antibiotic ver The dose of radon now ed is 15 mC in three seeds (in e earlier cases two seeds 10 mC re used) and maintenance rapy with cortisone (25 mg lly) is instituted Up to now ne cases of advanced cancer have en treated by this method without mortality or rbidity All the patients have complained of mild adache on the evening of the operation but in no stance has this persisted beyond the second post rative day In only one case was the convalescence mplicated by evidence of infection the patient's mperature suddenly rising three days after the implant his was rapidly controlled with aureomycin and no ganisms were isolated from the cerebrospinal fluid atients are ambulant the day after the implant, and are lowed home in six days

The progress of these patients is being followed nically radiologically and biochemically and the fect of the implant on certain endocrine functions being studied

The simplicity of this method allows its use in cases suitable for major surgery and we believe that it ay prove as effective as, but less hazardous than tal adrenalectomy and oöphorectomy Although so far this treatment has been used exclusively for advanced cancer it may prove applicable to pituitary hyperactivity

We wish to record our sincere gratitude to Prof C F W Illingworth for permission to treat these cases in his unit and for his encouragement in the development of this project to Dr A A. Charteris and his staff of the department of radiotherapeutics for their coöperation to Miss Ann Hendry superintendent radiographer Western Infirmary for her invaluable assistance with the radiographic technique and to Mr Angus MacDonald who constructed the director apparatus in the Western Infirmary Workshop

A P M FORREST
B.Sc Ch.M St And
F.R.C.S E F R.C.S.
Lecturer in surgery

D A PEEBLES BROWN
M B Glasg
Hall tutorial fellow

University Department
of Surgery
Western Infirmary
Glasgow

Medical Societies

ROYAL SOCIETY OF MEDICINE

Endocrine Response to Trauma

THE section of surgery met on May 4 under the hairmanship of Mr HAROLD EDWARDS the president o discuss Endocrine Response to Trauma

Prof FRANCIS D MOORE (Boston Mass) said that the ndocrine glands were the motors which drove surgical onvalescence, and study of their behaviour was not an cademic exercise but essential for the practical direction f surgical care

In response to the stimuli of pain fear, blood loss and ether anæsthesia there appeared to be pronounced adrenomedullary secretion not yet extensively studied by biochemical methods After trauma the blood level of corticotrophin rose and the blood level of compound F increased to four or five times normal Within sixty seconds of trauma the blood-corticoid level in the adrenal vein increased to a hundred times normal In addition sodium conservation occurred presumably as aldosterone was secreted but the changes in sodium and chloride metabolism did not coincide with the movement of nitrogen and potassium In addition this early phase was marked by alterations in water metabolism which might be due to the effects of antidiuretic hormone

After these early changes there was a period which resembled the withdrawal of adrenocortical hormones and was reflected in a decreased urinary output of corticoids and nitrogen It occurred within a few days of abdominal operations but later after fractures. This often involved a drastic reduction in urinary total nitrogen excretion from 12–15 g daily to 5 g or less.

There then followed a third phase—that of spontaneous anabolism This was the period of rebuilding It started about one week after pneumonectomy or gastrectomy and lasted three to five weeks. A patient weighing 70 kg accumulated 3–7 g nitrogen per kg per day The glands mediating this phase were thought by some to be the gonads but Professor Moore believed that growth hormone was more probably involved This had not been proved Finally fat replacement took place, ceasing when the patient reached normal weight

If the operation was followed by complications, such as sepsis, pulmonary embolus or wound dehiscence the secretion of corticoids increased again, even though they might have fallen from the initial postoperative high level.

Ether anæsthesia given to volunteers increased the blood-corticoid level but thiopentone did not. Moderate hæmorrhage of 770 ml blood did not cause increased corticoid secretion Alterations in corticoid levels and depression of circulating eosinophils of the same order as he had observed in surgical cases could be brought about in a healthy volunteer by the intravenous infusion of 25 units of corticotrophin

Prof G M WILSON (Sheffield) spoke about the postoperative fall in plasma sodium and chloride levels. If patients who had undergone partial gastrectomy for peptic ulcer were kept on a restricted water intake the plasma sodium and chloride levels remained steady for twenty four hours and then declined The decrease was not attributable to postoperative water retention alone and it was not easily related to any known aspects of adrenocortical or pituitary function It had been shown that interference with the temperature or oxygen supply of tissue slices caused movement of sodium and chloride ion from the medium into the cells.

Professor Wilson went on to discuss changes after bilateral adrenalectomy and ovariectomy for carcinoma of the breast The eosinophil-count fell but when the patient was put on 100 mg cortisone daily after operation the eosinophils rose again distinctly The plasma sodium and chloride decreased The urinary excretion of 17-ketogenic steroids was normal, increasing slightly when cortisone support was given, it rose greatly after operation, while the urinary 17-ketosteroids fell He had found similar changes in a patient maintained on 150 mg cortisone a day, although the urinary 17 ketogenic-steroid excretion did not change much after operation In these patients, maintained on a constant dose of cortisone, the urinary conservation of sodium and chloride was good in the postoperative period, even in the absence of the adrenal cortex Professor Wilson cautioned against the over-enthusiastic use of sodium chloride infusions in the postoperative period

Mr F W HOLDSWORTH (Sheffield) emphasised the importance of œdema of the wound as a cause of fluid-loss in injured patients Fluid-loss into the wound began two to three hours after injury and continued for two to three days In wounds of moderate size it was well tolerated and did not call for replacement, but in very large wounds, such as burns, replacement was necessary Direct blood-loss must be replaced quantitatively, though assessment of the amount lost was difficult and the usual clinical criteria, such as pallor, tachycardia, and fall in blood-pressure, might be misleading since these might be due to neurogenic causes even where there was little or no wound The most reliable guides to the quantity of blood lost were the size and type of the wound considered with the systolic blood pressure Replacement should be quantitative, for there was considerable danger associated with over trans fusion The presence of lacerated tissue had a profound toxic effect, so traumatic wounds must be excised as soon as possible The dangers of anæsthesia had probably been greatly exaggerated, but he considered that the preoperative nutritional state was very important

Mr L P LE QUESNE pointed to the dangers of adopting postoperative changes in urinary salt excretion as a basis for therapy The changes usually reflected natural metabolic changes in the body

Dr STUART MASON illustrated the effect of total hypophysectomy on the salt and potassium balance while the patient was maintained on a constant dose of corticotrophin (60 mg daily) and constant salt intake Similar data, together with nitrogen, phosphorus, and calcium balances, illustrated the effect of total adrenalectomy in a patient maintained on a constant dose of cortisone (80 mg daily) In both patients the metabolic response to trauma was similar to that found after operation on patients with intact adrenals The results supported Ingle's concept of the "permissive" rôle of the adrenal

Prof C H GRAY pointed out that by existing chemical techniques only a very small number of the steroids secreted by the adrenal cortex were estimated Furthermore since the adrenal cortex secreted at least five different hormones with three different kinds of function it was possible that the anabolic and katabolic changes after trauma were due to the secretion by the adrenal of different proportions of these substances

Replying to the discussion Professor MOORE said that adrenalectomised dogs receiving cortisone had a raised blood-level of corticoids If they were then anæsthetised with ether the corticoid level rose further, and ether anæsthesia and trauma combined also led to an increase He wondered whether this was due to failure by the liver to inactivate corticoids

The nature of the wound was more important in determining the metabolic response than in determining the endocrine response The mechanism of this seemed to be extra-adrenal

Hypothermia in dogs or man caused the blood corticoid response to be abolished, warming was followed by a delayed response

Reviews of Books

Multiple Sclerosis

DOUGLAS MCALPINE, M D, F.R C P, physician-in department for nervous diseases, The Middlesex Ho NIGEL D COMPSTON, M.A, M D Camb, M R.C.P., physician, The Royal Free Hospital, London, Car LUMSDEN, M D Aberd, Sir Henry Head Research of the Royal Society Edinburgh and London E Livingstone 1955 Pp 304 35s

To produce a 300-page volume on a single dis not without hazards On the one hand it is questi whether the intrinsic interest of disseminated sc as we now know it is sufficient to compel the con attention of the expert On the other hand, the stu or the clinical dilettante is unlikely to devote a seem disproportionate amount of time to the contemp of clinical pleomorphism We therefore greet monograph by Dr McAlpine and his colleagues mixed feelings

It consists of a global account of the disease derived experience of over 1000 cases seen at the Middlesex Ho during some twenty two years The first and larger p the book deals with details of clinical history, geogr factors, accessory clinical findings, and the problem diagnosis, prognosis, and management It is readably clearly written, and it is undoubtedly of value to have mass of information collected into a single book with statistical evidence on prognosis and on variation in composition of the cerebrospinal fluid The section differential diagnosis should help the general physician, may, however, be surprised to find an essay on cer spondylosis included in this chapter The review of pre day management is practical While recognising the me of specific therapy, it shows how much can be achieved long-term management An unexpected enthusiasm intravenous neoarsphenamine and liquor arsenicalis possible minor blemish in this balanced report

The second part of the book is mainly on pathology, some interesting excursions into demyelination, to wh Dr Lumsden's experimental work has clearly contribute largely This section includes some excellent photogra The final chapter on ætiology, though it contains noth new, sets out clearly and concisely the present proble By these qualities it is characteristic of the wh volume

Crime Detection

Modern Methods of Criminal Investigation ARN SVENSSON, assistant, OTTO WENDEL, chief assista National Institute of Technical Police, Stockh Amsterdam and New York Elsevier Publishi Company London Cleaver Hume 1955 Pp 38s 6d

THE considerable success that attended the appeara in 1949 of the Swedish *Handbok I Brottsplats Unde sökning* fully justified its translation into English, a the two authors—technical and police experts at the National Institute of Technical Police in Stockholm have wisely broadened the scope of the text for inte national reading It has been so substantially revised and superbly illustrated from the authors' own crime fil as to constitute a new book in clear impeccable Engli and remarkably comprehensive within a comparativel small space, it is undoubtedly the best practical gu to crime investigation we have yet seen

The authors carefully avoid elaborating the mo difficult bench techniques—those of blood grouping, instance—that have by now been passed to experts in serology, but they do not fail to indicate where to loo for blood at a scene of crime, how to preserve the m material, and in what respects it may be tested Print hairs, fibres, dusts, glass, wood—all receive authorita treatment, and there is a remarkable piece of writing Svensson on firearms and explosives

In use the book is sound and really practical C I D office, no crime laboratory, and few unive departments of forensic medicine could fail to pro greatly by constant recourse to this short but comp

nsive guide to technical police methods It is a
ne tribute to the respected institute from which it
nnes.

ypertension and Nephritis

5th ed ARTHUR M. FISHBERG M D director of medicine Beth Israel Hospital New York. London Baillière Tindall & Cox. 1954. Pp 986 £5

"Fishberg" needs no introduction as an exhaustive nd valuable bibliography on hypertension and nephritis. n the fifteen years since the last edition progress in this ubject has been both deep and wide The main advances nclude clearance studies of renal function and extensive esearches on the relationship between the kidney and ypertension These on the one hand have led to new peculations on the genesis of renal hypertension and n the other hand have helped to clarify the classification f Bright's disease New light has been thrown on specific iseases of the kidney, especially diabetic glomerulo clerosis, chronic pyelonephritis, and tubular necrosis. pecific tubular disorders leading to electrolyte disturbnces have been discovered Dr Fishberg's summary of ecent work on these subjects, and his references, are an xcellent starting point for anyone requiring further nformation He still regards chronic lipoid nephrosis as n entity and gives inadequate weight to the recognition nd differentiation of type-1 and type-2 nephritis. In view of the numerous drugs now available for the reatment of hypertension, it is welcome to find a warning n this section that many individuals not only need no reatment, but are much better off without it'

An Atlas of Operations for Trauma

OTTO RUSSE Vienna and Bonn: Wilhelm Maudrich for Medizinische Wissenschaften. 1955 Pp 100 DM. 50

THIS Atlas, with its 48 full page plates, and text in German, French, and English, is elegantly got up; the translations are adequate and the pictures are clear But it is a pity that some of the operations so well depicted are culled from the world literature with no assessment of their feasibility or value The illustrations include methods of purely historic interest, such as the use of 'pinch grafts, and equal emphasis is placed on procedures that are established, questionable and even just imagined Oversimplification has led to attention being focused on bone injuries to the neglect of the associated soft tissues, in relation both to repair and to the surgical approach Thus the skin incisions shown are entirely orthodox and take no account of the need, at the acute stage of injury to preserve undamaged soft tissues. The methods of treatment required at the emergency stage are not distinguished from those of value at a later stage of reconstruction In resuscitation blood transfusion is mentioned on a par with subcutaneous saline To present so much in so small a space is necessarily very difficult and in this Atlas we feel, the diagrammatic approach has unfortunately made the surgery of trauma seem more a matter of skilful carpentry than of applied biology

Biochemistry of the Aminosugars

P W KENT M.A B.SC., PH D., D.PHIL. F.R.I.C; M W WHITEHOUSE B.A. B.SC A.R.I.C department of biochemistry University of Oxford London Butterworths Scientific Publications. 1955 Pp 311 40s

To those who think of plants and animals in terms of proteins, fats, and carbohydrates, the presence in the body of sugars containing amino groups may come as a distinct surprise They are as it were neither fish, fowl nor good red herring yet they are present in the skeleton, in mucins in the substances responsible for the blood-groups in the serum globulins in antigens, in antibiotics, and in chitin—in short in almost every walk of life They may appear as monosaccharides or polysaccharides and they may combine with proteins and lipoids in the most variable proportions They owe their construction form and function during life to a series of enzyme systems which maintain them in their steady state by a process of active metabolism. This book is the first comprehensive attempt to describe them since Levene's classical monograph in 1925.

The first part covers the biological associations of the amino sugars their metabolism, enzymic degradation their rôle in chondroitin heparin and chitin, and their share in the construction of the various mucins. There is a chapter on bacterial and fungal products which, as might be expected, are widespread and important To those who have been the victims of a severe pyrogenic reaction it may be of some interest if not perhaps comfort to know that their misery was due to an amino polysaccharide

The second part of the book deals more specifically with the chemistry of these amino components. It describes how they may be detected and isolated and goes into their structure, synthesis and reactions so far as they are known at present Glucosamine receives the most extensive consideration but galactosamine has a chapter to itself and another chapter is devoted to the hexoses with two amino groups. The fructose mannose xylose arabinose and inositol compounds are left to the concluding chapters. A considerable number of references are given after each chapter and there is a short postscript at the end of the book to bring the literature up to date at the time of going to press

The authors are to be congratulated on having produced a book that is both interesting and a notable work of reference.

The Digital Circulation

MILTON MENDLOWITZ, M.D F.A C P, associate attending physician, Mount Sinai Hospital, New York. New York Grune & Stratton. 1954 Pp 182 $6 75

IN this short monograph Dr Mendlowitz surveys the remarkably complicated subject of the digital circulation in health and disease, to which he himself has devoted much effort. Clubbing a teasing subject which has greatly attracted him, is as well discussed in a single chapter as it could be The theory of its ætiology, "an attempt to point the way is at least as reasonable as any other, though even Mendlowitz finds some difficulty in explaining the clubbing that accompanies intestinal disease and cirrhosis. A comprehensive list of references, numbering over 600 gives just credit to the pioneers in the study of the subject.

Retropubic Prostatectomy

For Benign Enlargement of the Prostate Gland. FRANCIS A BENEVENTI M.D F.A C.S., attending urologist, Oswald Swinney Lowsley Foundation St Clare's Hospital New York Springfield Ill.: Charles C Thomas Oxford Blackwell Scientific Publications. 1954 Pp. 227 60s

ALMOST ten years have elapsed since Millin introduced his retropubic approach to the surgery of prostatic obstruction but despite the wide adoption of the technique in the British Isles and Europe, American urologists have largely remained faithful to the transurethral methods. Dr Beneventi of New York, has given us the first transatlantic book on the subject, a beautifully produced work with many outstanding drawings by Mr W Didusch.

The anatomy of the prostate and surrounding structures is capably dealt with, though some of the photographs might have been omitted without much loss. The chapters on preoperative and postoperative management are thoroughly good and do not advocate unnecessary investigations Not everyone however will agree with the author's practice of 15 minute bladder irrigations in the early postoperative period The technique of the operation for enucleation of simple adenomata differs little from that employed in Britain though many will cavil at some pronouncements based apparently on a relatively small experience of 100 cases. It is difficult for example to accept that retropubic prostatectomy for the small gland is not feasible as the dense lateral plexuses of veins leave little room for exposure or that a bladder neck which will admit the tip of the middle finger following enucleation requires no plastic enlargement No mention is made in this connection of the hypertrophied trigone Dr Beneventi admits that he makes no attempt to secure a watertight closure of the prostatic capsule and accordingly leaves the urethral catheter (a modified Foley type) in for 6–7 days; his high incidence of meatal stricture (7%) may possibly be related to this practice Some 23 pages are devoted to osteitis pubis but the author concludes that the incidence of this complication is no greater after the retropubic operation than after operation by other method No mention is made of the occasional involvement of the vertebral bodies

Despite such minor criticisms the work will undoubtedly appeal to urological surgeons

Geisteskraft und Geistesstörung im Alter

Ärztliche Betrachtungen zum Altersproblem A KIELHOLZ, W A STOLL A L VISCHER, H WALTHER BÜEL, J WYRSCH Zürich Art Institut Orell Füssli Ag 1954 Pp 45 Fr 3 60

THIS collection of essays from Switzerland on psychiatric problems of old age is of some interest for the glimpses *it provides of work in this field on the Continent*

Most of the contributors make the descriptions of Kraepelin *and Bleuler the starting* point of their analysis of mental illness in old age, but these are inadequate when approaching the social and psychological problem of ageing with which contemporary psychiatry is faced To fill the gap some *authors go to Selye for* inspiration, others to Shakespeare's *King Lear* and the portraits of Rembrandt The essays however, reflect an approach to the psychological problems universal among old people in urban communities that is more practical and in keeping with human dignity than the formulations of some schools of psychopathology The style is rambling, and many of the sentences are of breath bereaving length, and some may feel that the effort required of the *reader is* disproportionate to the number of useful statements

New Inventions

PILOT TUBE FOR BLOOD BOTTLE

OPINION is still sharply divided as to whether a pilot tube is a safe and reliable accessory to a bottle of blood Some object to it on the grounds that, since it is not an integral part of the pint bottle, some change-over may occur, either at the donor session or later, whilst others consider that the bottle must in any case be sampled so that a stained smear may be examined to exclude the presence of bacteria

However valid these objections may be, there is no doubt that the risk of infecting the bottle at the time of sampling is a serious one Even though the most careful and aseptic technique is used (perhaps questionable when carried out by junior staff at night or in emergency), the blood must be transfused within twenty-four hours or not at all This advice, given by the Ministry of Health in "Notes on Transfusion," if rigidly adopted, must impose a strain on the blood-bank. It is often necessary to have several pints standing by for a patient for two or three days, and it is also not always easy to switch any unrequired cross-matched blood to another case within twenty-four hours

Examples of transfusion reactions known to be due to infected blood are happily rare, and although the routine preparation of a stained smear from the bottle is excellent in theory it is not always practicable If this additional test is considered necessary, the best time to do it seems to be immediately before the transfusion is set up, cross-matching having been done some time previously with the aid of a pilot tube

It is to overcome these objections to the pilot tube that the following design, method of attachment, and filling procedure, have been extensively tried and now adopted in the area served by the Sheffield Regional Transfusion Centre The tube, of 4 ml capacity, is more like a small bottle because it has a neck with a screw thread and is closed by a metal cap, having a central hole under which lies a rubber bung (fig 1) The base is rounded to give strength and, it is hoped, to act as an additional deterrent to removal, since the bottle will not stand on a flat surface

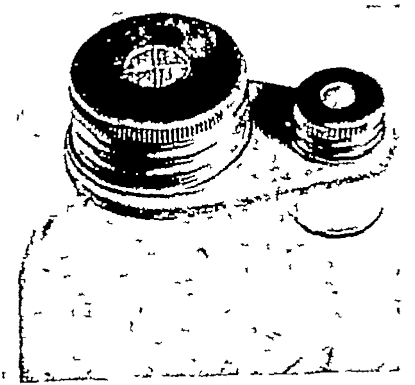

Fig 1

The attachment consists of an aluminium strip flanged *round the edge to give greater rigidity and* perforated by two holes The diameters of these are such as to allow the strip to pass over the screw threads of both bottles but no further Both the bottles are firmly united when *the caps are screwed home, and* no accident or careless handling can separate them A label is therefore considered superfluous, for, even if the smaller cap is removed, which is contrary to instructions, the shoulder *of the large bottle prevents the* pilot bottle from slipping through

Fig 2 illustrates the method of filling the pilot bottle at the donor session in three stages, A, B, and C, the whole process being completed immediately after venesection and before the pint bottle joins those from other donors The lengths of tubing in the taking sets shown have been shortened for the sake of clarity A is a unit ready for use, with the donor's *needle protected* by a shield until the moment of venepuncture. The vial attached by an elastic band is retained, when filled, at the transfusion centre for grouping and Kahn testing

B shows the unit after venesection The *tubing* is clamped, and the needle is withdrawn from the arm and inserted into the vial, which now carries a label with a serial number corresponding to that on the large bottle C shows the needle X *transferred to the* pilot bottle, which fills easily, after the clamp is released, having been vacuumised before sterilisation

The simplicity of this final movement, and the close attachment of the small bottle, *effectively* prevent the possibility of error or confusion

The pilot tube is manufactured by the International Bottle Company, 140, Park Lane, London, W 1, and the aluminium attachment by the Wolf Safety Lamp Co (William Maurice Ltd), Saxon Road Works, Sheffield, 8

J S CAMPBELL
M.R C.S

Sheffield Regional Transfusion Centre

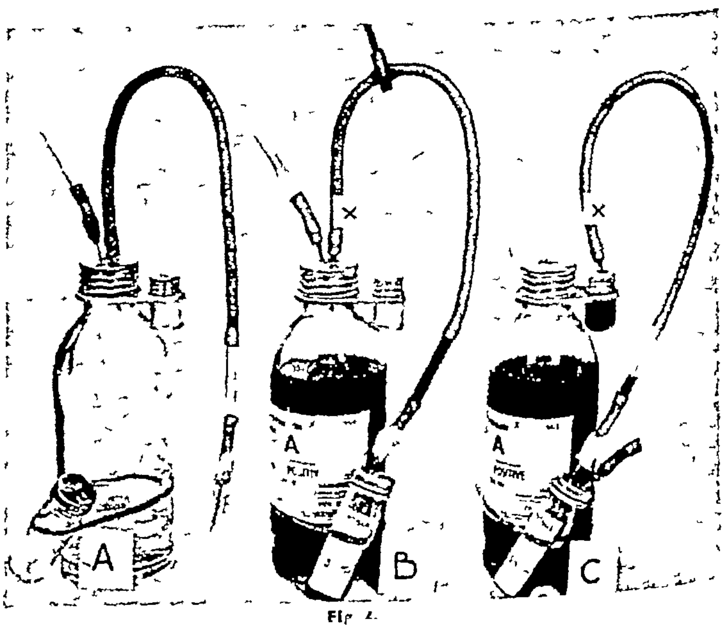

Fig 2

THE LANCET

LONDON SATURDAY MAY 21 1955

Abuse of Antibiotics

LAST October 172 speakers contributed to the second Annual Symposium on Antibiotics[1] In opening the discussion, Dr HENRY WELCH not unreasonably said that it would take too much time o list the infectious diseases now partly or completely controlled by chemotherapy, instead he remarked that few of his large audience would not have some friend or relative who had been made well, or even been saved from death, through the use of antibiotic drugs There was much to justify President EISENHOWER's message to the symposium in which he described the meeting as an occasion for honouring all who through their work on antibiotics had made profound changes in the practice of medicine Those honoured would rightly include not only medical and scientific investigators, but also the drug firms whose energy and enterprise made possible the necessary research and development on a vast scale

With all this we are already familiar But, owing largely to our own folly the picture has a less favourable aspect VON OETTINGEN,[2] reviewing the untoward effects of the indiscriminate use of antibiotics, noted the possibility of such well authenticated complications as glossitis and stomatitis, nausea, vomiting, and diarrhœa anal pruritis, vestibular and auditory disturbances, aplastic anæmia, and allergic reactions of many kinds, including fatal anaphylactoid reactions serum-sickness, and skin rashes Admittedly most of these reactions are relatively uncommon in proportion to the widespread use of antibiotics, and most are temporary but enough of them may produce serious damage and even fatal results to justify an earnest plea for caution against uncritical use of antibiotics Apart from the danger to the patient such indiscriminate use must accelerate the emergence of resistant strains of bacteria among species which produce such forms This has been said many times in these columns and elsewhere, indeed it has been emphasised so often that its rehearsal may fall on deaf ears It may have been some such thought that led HUSSAR[3] to propose a more active measure—a crusade for the rational use of antibiotics In his own analysis of fatal antibiotic reactions he showed that about half of the patients had died from unnecessary medication. He estimated that about 25% of patients in the medical wards of general hospitals would probably benefit from antibiotics This figure was very close to that observed in three hospitals where strict indications had been set up for the administration of antibiotics But in three other hospitals the proportions of general medical patients treated with antibiotics were 32%, 38% and 41%, and in HUSSAR's view these higher figures reflect a too liberal use of antibiotics He proposed (1) a press release from the symposium condemning the irrational use of antibiotics, (2) systematic education of students and doctors on how to use antibiotics, (3) education to persuade the lay public that antibiotics are not invariably required, and (4) organisation of a National Registry of Fatal Antibiotic Reactions to reveal the true incidence of such accidents

What errors of judgment and practice have given rise to these sobering pronouncements? Three seem to deserve prominence First, there is a belief that antibiotics are non toxic and will do no harm even if they do no good It is easy to see how this view arose Penicillin our first antibiotic, had a much greater margin between effective and toxic dose than any previous antibacterial drug and untoward reactions were virtually unknown in the early days when it was administered in doses of the order of 15 000 units every four hours Only when very much larger doses came to be used—at first for special cases but later almost as a matter of routine—and when sensitised patients came for second courses of treatment did it become clear that the drug was not altogether harmless Later antibiotics are in general more toxic than penicillin and so allow less latitude in dosage The second defect in our thinking touches this very point Many doctors are guided by the popular but fallacious generalisation that if a little does good a lot will do better Many considerations doubtless combined to foster the use of big doses they were required for bacterial endocarditis, they were *bactericidal*, they would stop the emergence of resistant strains, they would make for less frequent administration, and they would penetrate to the deepest parts of hidden lesions Such considerations neglect two essential points that many antibiotics have a relatively narrow zone of optimal concentration,[4] and that the doses recommended by manufacturers are the outcome of extensive pharmacological and clinical studies As MENNIE[5] has rightly declared clinical investigators should aim at determining the smallest amount that is effective therapeutically One may smile at the plea for chairs of antibiotic medicine voiced by more than one speaker at the symposium but the surest way to encourage such projects is to give antibiotics so heedlessly as to create the impression that yet another specialty is required

The third wrong idea—inside as well as outside hospitals—is that since antibiotics are so dramatically effective against grave illnesses they will be at least equally useful for the treatment of minor disabilities But many conditions with an infective component—for example some skin diseases and chronic disorders of the cardiorespiratory systems—cannot be regarded as wholly or even mainly caused by infective agents On the whole antibiotics are disappointing in the treatment of such states, and the most probable outcome of their use is sensitisation of the patient, who disseminates resistant staphylococci For much the same reasons the so called prophylactic use of antibiotics is very often unwarranted It will be a bad thing if it comes to be regarded as a token of eccentricity or of over-confidence to do a deliberate surgical operation without "antibiotic cover" COURT and his colleagues[6] emphasise the crucial fact that the more frequently the staphylococci in a particular community are exposed to a particular antibiotic, the more likely they are to become resistant to it They reversed their earlier policy of treating with penicillin all staphylococcal infections in the newborn, and have had no cause to regret their decision no serious infection, such as pneumonia or osteitis, developed in any of the 633 babies with a superficial infection who were treated on conservative lines which precluded the use of antibiotics in the absence of some good clinical indication, such as evidence of a systemic infection They have kept erythromycin in reserve for the patient whose life may depend on it Dr FORFAR and his colleagues, whose letter appears on p 1071, use antibiotics somewhat more liberally but no less rationally How many others who prescribe antibiotics would care to defend their practice ?

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[1] Antibiotics Annual 1954–1955 Proceedings of the Second Annual Symposium on Antibiotics Edited by HENRY WELCH, PH D and FELIX MARTI-IBAÑEZ, M.D New York Medical Encyclopedia, Inc 1955 Pp 1145 $10 00

[2] von Oettingen, W F *Ibid* p 361

[3] Hussar A E *Ibid* p 3 9

[4] Gunnison, J B., Kunischige E., Jawetz E. *Ibid* p. 190

[5] Mennie A T *Brit med. J* April 16 1955 p 973.

Disseminated Sclerosis

SINCE the late war there has been gratifying progress in our knowledge of disseminated sclerosis This is due largely to the efforts of laboratory workers, but, as Dr MCALPINE shows in his Florence Tong lecture published in this issue, clinicians and field-workers have contributed much and may contribute much more In this disease with its protean symptoms, lengthy and varied course, and lesions that may be closely mimicked by other disorders, confusion in diagnosis is inevitable For this reason many early surveys of incidence have to be discounted, and there is now a need, as MCALPINE shows, for more accurate statistics in this and other countries

The high prevalence-rates in Northern Ireland[7] and northern Scotland, particularly the Shetland Islands, give much food for thought KURLAND et al[8] believe that prevalence is determined by geography rather than by race, the disease apparently being relatively rare in tropical countries it is, for instance, six times less common in New Orleans than in Winnipeg The Winnipeg rate is essentially the same as that for Boston, and is not much in excess of that for Denver, but both Boston and Denver have mean January temperatures considerably higher than that of Winnipeg As KURLAND and his colleagues remark, the prevalence-rate seems to increase rapidly as the winter temperatures drop, but after the "cold" weather areas are reached still lower temperatures cause no appreciable increase Once the disease is established temperature seems to have little effect on its course, for the life expectancy of patients is about the same in Winnipeg as in New Orleans SWANK et al[9] chose for their investigation rural Norway, because of its many isolated communities who for their food depend largely on their own resources They found a much higher incidence in the upland farming and dairying areas than along the coastal belt where fishing is the principal industry In the relatively prosperous farming districts they noted that the diet was richer in fat, particularly milk and animal fat, but they remarked that this greater consumption of fat might coincide with other factors having the same distribution In their studies they made use of true incidence figures as reported to them by neurologists and hospitals, for prevalence figures, being influenced by the duration of the disease, may not always indicate true differences in incidence Support for the view that an excessive intake of fat may be a factor in ætiology has not been forthcoming A priori, the quest for a dietary deficiency or for a cytotoxic contaminant might be expected to prove more profitable than investigating the effects of a surfeit of any foodstuff DE MORSIER and CHESNI[10] have described seven siblings, three of whom were employed as painters one died of tuberculosis, and in the other two disseminated sclerosis developed at the age of forty-two SHIELD,[11] noting a high incidence of disseminated sclerosis in those parts of the world where the land is intensively cultivated, has questioned whether inorganic fertilisers remedy acquired deficiencies in the soil The possible far-reaching effects of the "sophistication" of foods, and especially of dietetic insufficiency in early life, have been discussed by PLATT,[12] who calls for an investigation into the composition of the cerebrosides of myelin in the infant's nervous system, with special reference to changes in their composition as a result of substituting cow's milk (which is relatively deficient in lactose, and therefore in galactose) for human milk If, he asks, glycocerebrosides are substituted for the normal galactocerebrosides, do they persist into adult life, and if so are they more readily hydrolysed than the galactocerebrosides ? There is, as yet, no evidence that galactose is synthesised elsewhere than in the breast On the other hand, it is believed that throughout life there is a constant turnover of myelin and that the oligodendrocytes are probably concerned in this maintenance work An environmental factor such as this might not easily be reconciled with the rarity of the disease in each of monozygotic twins[13] but it would offer an alternative to the genetic explanation for familial cases PRATT, COMPSTON, and MCALPINE[14] report a family history in 6 5% of cases, and believe that this constitutes some support for the view that a genetic factor is at work According to KURLAND and his associates, however, the magnitude of the discordance in monozygotic twins rules out a simple genetic factor

MCALPINE, COMPSTON, and LUMSDEN,[15] in drawing attention to the hypothesis of oligodendroglial lysis, suggest that the objective should be not so much to determine the cause of the demyelination as to ascertain why there has been interference with the normal process of myelin resynthesis, but if in the sease there is an inherent failure on the part of the godendrocytes to resynthesise myelin, this still does t explain the focal distribution of the lesions, and he slowly expanding areas of demyelination multiple d often confluent, which apparently spread from nules The special vulnerability of the optic athways in disseminated sclerosis[16] and in the osely related condition of neuromyelitis optica has so to be explained It is evident, therefore that ttention must continue to be directed to a search for yelinolytic and probably oligodendrolytic agents as ell as to the blood vessels whose rôle remains obscure istological studies of the venules have been relatively rewarding and more precise methods for investi ating the vascular dysfunction in the nervous stem are needed. Fog et al[17] adduce evidence to how that the blood platelets are decreased during the tive phases of disseminated sclerosis, rising again, as n infections, during recovery They attribute the ll to an increased consumption of platelets during he active phase and suggest that this is part of a eneral reaction to the disease process. NATHANSON nd SAVITSKY[18] found that platelet adhesiveness is ncreased during periods of activity Other evidence ointing to a general reaction has been reported by ERNSOHN and COCHRANE[19] and VOLK et al.[20] VOLK t al have found an increase in the α_2 and β globulin believed to be the main lipid containing fractions of he plasma) in over three quarters of the cases they tudied, but since these findings were especially ommon in cases of long standing they deduce that he protein changes in the cerebrospinal fluid—commonly consisting in increase of the γ globulin—antedate the changes in the serum The early increase in γ globulin in the cerebrospinal fluid is believed to mply the establishment of an acquired immunity mechanism In this connection the premonitory symptoms, especially when these include a disturbance of general health deserve further careful study, as do also the transitory and sometimes almost momentary symptoms of some patients whether these are due o vasospasm, as FRANKLIN and BRICKNER[21] postulate, or increased vulnerability of the axis cylinders to chemical influences as MCALPINE suggests or even by both is undecided Study of the evolution of the symptoms may help not only to locate the lesions but also to assess their rate of progress MCALPINE[22] has shown that the mode of spread of paræsthesiæ is often in keeping with our ideas of focal diffusion

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[6] Court S D M , Green C A , Hutchison J G P , Neligan G A *Lancet*, May 7, 1955 p 969

[7] Allison R S Millar J H D *Ulster med J* 1954, 23 suppl 2 See *Lancet*, 1954, i 1334

[8] Kurland L T Mulder, D W Westlund K B *New Engl J Med* 1955, 252 649

[9] Swank R L , Lerstad, O , Strom, A , Backer, J *Ibid*, 1952, 246 721

[10] de Morsier G , Chesni, Y *Schweiz med Wschr* 1952 82, 41

[11] Shield J A *Sth med J* 1947, 40 56

[12] Platt B S *Brit med J* Jan 22 1955 p 179

[13] Thums K *Wien Z Nervenheilk* 1952, 4 173

[14] Pratt, R T C Compston N D McAlpine D *Brain*, 19 74 191

[15] McAlpine, D Compston N D , Lumsden, C. E. Multiple Sclerosis Edinburgh 1955

Thanks to improved and earlier diagnosis careful attention to the general health, and prophylactic treatment of complications, the prognosis of this disease has improved and the average duration of life after diagnosis now exceeds twenty years RIESE and his associates[23] have reported necropsy findings on a seventy five year old man with classical symptoms of this disease first diagnosed as such fifty years earlier by Sir WILLIAM OSLER

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[16] Lehoczky T Acta morph Acad sci hung 1954 4 395
[17] Fog T, Kristensen I, Helweg Larsen H F Arch Neurol. Psychiat 1955 73 267
[18] Nathanson M, Savitsky J P Bull N Y Acad Med 1952 28 462
[19] Bernsohn J, Cochrane L S G Proc Soc exp. Biol N Y 1951 86 510
[20] Volk B W, Saifer A, Rabiner A M, Oreskes I Arch. Neurol Psychiat 1955 73 68
[21] Franklin C R, Brickner R M Ibid 1947 58 125
[22] McAlpine D Arch. Middlx Hosp 1954 4 1
[23] Riese W, Jones O L, Last, I G, Bramer-Maxwell L, Doel H L Confin neurol Basel 1954 12 113

Better Nutrition

ONE of the most useful of the expert committees serving the World Health Organisation is the one jointly established with the Food and Agriculture Organisation to keep nutritional problems under review At its recent meeting the Executive Board of W.H.O. paid tribute to the excellence of the report of the committee's session last October,[1] when Prof B S PLATT presided and Dr NORMAN WRIGHT represented the Ministry of Food This report, it was felt, happily illustrated coöperation both between F.A.O. and W.H.O. and among national authorities

It is satisfactory to find protein requirements getting further close attention, for, though protein malnutrition is now recognised as a serious cause of ill health among women and children in most tropical and subtropical countries the amount of protein necessary for good health in various circumstances is still a matter on which opinions differ and evidence is insufficient Further investigation is needed too, on the development of protein rich foods for the supplementary feeding of breast-fed infants and for weaned infants in parts of the world where at present human milk is the only suitable form of protein the child can get Besides additions to diets, there is also the question of additions to foods, and the report considers, for example, proposals to add vitamin A to dried skim milk and to add potassium iodate (which is less liable to loss than the iodide) to the salt consumed by the inhabitants of goitrous areas[2] Equally important in their own way may be those additions to food which are made for the benefit not of the consumer but of the seller, and a section entitled 'Additives to Foods" is primarily concerned with such intentionally added non nutritive substances. The point made is not that any of the substances discussed are known to be harmful to human beings, but that a large proportion of them are not known to be safe Evidently opinions differ widely about many of the additives in common use for the report says that while twenty two countries permit the addition of certain specific colours in foods only 1 out of 82 such colours is permitted in all twenty two countries Furthermore it would be wrong to suppose that the only countries affected by these practices are those where technology is highly developed and where the consumer demands highly attractive foods, uniform quality, and a wide choice at all seasons addition of preservatives, for example, may be an important matter for countries which are economically and technically less developed but are situated in tropical or subtropical regions where food preservation entails special difficulties When foods enter as commodities into international trade it is particularly desirable in the committee's view that there should be international pooling of knowledge

Probably most of the accessory food factors essential in human nutrition have now been identified, but, though beri beri and scurvy have been degraded from major menaces to preventable nuisances, it has become plain that there are many foods with properties besides the absence of vitamins which are capable of contributing to ill health Opinion on the causes of pellagra, which formerly favoured a toxin in maize, shifted to nicotinic acid deficiency, but has now reverted to the idea that even if maize contains no specific toxin it has at least some positive dietary disadvantage when ingested in very large amounts The expert committee did not perhaps pay quite enough attention to the relation—in areas where a great deal of maize is eaten—between different maize-processing methods and the prevalence of pellagra The absence of pellagra from Mexico, where maize is prepared as *tortillas*, was mentioned, but nothing was said about the fact that it is also absent from areas of Africa which subsist mainly on maize prepared according to traditional methods, and that in many areas it has appeared since the introduction of dry-milling machinery Experiments at Cambridge and Reading which have lately been recorded in our columns[3] lend strong support to the opinion that a great deal depends on the method of preparation

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[1] Joint F.A.O./W.H.O. Expert Committee on Nutrition: Fourth Report W.H.O./Nut/55 Nov 15 1954; Tech. Rep. Wld Hlth Org (in the press)
[2] See Scrimshaw N S, Cabezas A, Castillo F, Mendez J Lancet 1953 ii 166

In the past it has sometimes been assumed that nutritional problems will be solved by education, that feeding will automatically become adequate if instructions are followed implicitly It remains true, of course, that education is one of the most instruments of nutritional work, but it is also one of the hardest to use properly Difficulties arise not so much over the methods of teaching as over the content of what is taught The practical steps people can take to improve the level of their nutrition differ enormously from one region to another, and if the public fail to obey when exhorted to adopt changes which have proved beneficial elsewhere, but are quite impracticable in their own area, it is not they but their instructors who are at fault The W H O/F A O report emphasises the need for doctors and nurses to be told more about nutrition in their training, and certainly many of them work in circumstances where a good general knowledge of the subject is almost a first essential But it is vital to ensure that the instruction they will give relates to the actual dietary habits of the country in which it is to be applied, and not simply to those of the countries which produce most of the textbooks

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[3] Braude R Kon, S K Mitchell K G Kodicek E *Ibid*, April 30, 1955 p 898

Annotations

MARFAN'S SYNDROME

THE condition originally described by Marfan[1] as dolichostenomelia was apparently a congenital abnormality of the skeleton characterised by the length and slender proportions of the long bones The alternative title of arachnodactyly was introduced by Achard[2] to emphasise the "spider-like" appearance of the hands The syndrome is now taken to include various ocular abnormalities, of which subluxation of the lens is the commonest, and cardiovascular lesions, of which aortic dilatation and dissecting aneurysm are probably the most usual and are certainly the most serious

Achard first drew attention to a hereditary and familial tendency, but according to Rados[3] the family history was positive in less than 40% of cases McKusick[4] has now re emphasised the importance of heredity in the genesis of the syndrome An inquiry into the kinships of 50 unequivocal cases revealed a total of 105 affected persons, excluding many doubtful cases Of the relatives of all the available patients with subluxation of the lens, 70% had recognisable stigmata of the syndrome The genetic data indicate that the disease arises as a result of a single mutant gene which is subsequently transmitted as a dominant McKusick concludes that about 15% of all cases arise from such a mutation and 85% by transmission

The large number of tissues and structures that may be affected in Marfan's syndrome suggests that if a single defect is responsible this must be fundamentally important Its nature is by no means clear, from the microscopic appearance of cystic medial necrosis, which is the usual finding where the aorta is dilated or has undergone aneurysmal dissection, McKusick concludes that the elastica is probably the tissue primarily affected But it is difficult to see how such involvement can be responsible for the various ocular and skeletal abnormalities "unless one assumes that the presence of this defect during embryogenesis produces an abnormal setting in which these particular anomalies occur with increased incidence"[4] In any event the fundamental defect is functional rather than structural, at least in so far as it affects the aorta What is inherited is apparently an inability of the elastic tissues to withstand the normal wear and tear of life Consequently the patient may in childhood show no evidence of cardiovascular abnormality, but in adult life have severe aortic dilatation, valvular incompetence, and myocardial hypertrophy[4]

The presence of an underlying biochemical defect is strongly suggested by the production in rats fed on the seeds of *Lathyrus odoratus* of a syndrome that includes skeletal defects and degeneration of the media of the aorta leading to dissecting aneurysm[5] An active principle recently extracted from the seeds of *L odoratus* is β amino propionitrile Lathyrism in rats cannot justifiably be regarded as a phenocopy of Marfan's syndrome But the striking similarity of many of the features of these two conditions does support the view that the complex anomalies that make up the syndrome in man are based on a single transmissible biochemical defect

DOCTOR, NURSE, AND HOSPITAL

SOME twenty five years ago Dr G O Barber, who had then been two years qualified, saw a district nurse for the first time—as a pair of black stockings emerging from a low gipsy tent He had heard of her for the first time about ten minutes before, when she had telephoned to him to come and help with a difficult confinement She crawled out of the tent, and he crawled in, and in due course the baby was born In recounting this incident at a conference on the link between hospital, general practitioner, and the district nursing service, arranged by the Queen's Institute of District Nursing and held in London on May 12, he said how astonishing it was—and still is—that a medical student can complete his training and go into general practice without hearing a single mention of one of the most important members of his team His own efforts to remedy this defect are well known[7] he was the first to suggest and help to put into action the plan, now flourishing in several medical schools, of sending medical students to spend a week, during their last year of training, in the household of a general practitioner There they learn something of the work he does, and the people who help him to do it Otherwise, as Dr Barber pointed out, they get no chance, in the course of their training, of learning bout the long lives of patients before and after they me into the wards "They learn only the little chunk f illness that the patient has in hospital" In his own artnership the link of the doctors with all six of the urses in their district is strong: he and his partners ieet all of them at least once a week—either over a case, r over the telephone or when a nurse calls into the urgery, or a doctor calls in on a nurse to discuss a case r exchange information The nurses not only know iore about the social background of the patients than nybody else: they also know all their doctors but he dmitted that this is managed more easily in the country here doctors are relatively few than in the owns where a nurse may need to get to know 60-70 loctors

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[1] Marfan A B *Bull Soc méd Hôp Paris*, 1896, 13 220
[2] Achard, C *Ibid*, 1902 19 834
[3] Rados, A *Arch Ophthal Chicago* 1942, 27, 477
[4] McKusick V A. *Circulation*, 1955, 11, 321
[5] Goyette, E M., Palmer P W *Ibid*, 1953 7, 373
[6] Ponseti, I V Shepard, R S *J Bone Jt Surg* 1954, 36A, 1031
[7] *Lancet* 1952 i, 495

In comparison with the strong link of the general ractitioner with the district nurses his link with the ospitals is often weak and sometimes non-existent. Miss R Bonsey, deputy head almoner at St Thomas's Hospital suggested that it might be strengthened through her own department The district nurse should keep in ouch with the almoner and seek her help in the aftercare of patients especially if the illness has caused financial difficulties It is natural she said when a patient's physical state deteriorates for his doctor to seek the help of the hospital: it should be equally natural, when his social state deteriorates to seek the help of the almoner Miss D M Williams superintendent of the District Nurse's Home at Plymouth had some excellent recipes for keeping doctor district nurse, and hospital aware of each other, the basic ingredient being intelligent explanation, and the prevailing flavour her own fresh and friendly wit. After eighteen years in one place she does know at any rate as voices on the telephone the general practitioners—all 75 of them—with whom her nurses have to work. Nowadays, she said the district nurse does for the doctor many things he used to do himself—such as giving injections to diabetics She can help him best if he knows how her work is arranged and part of a nursing superintendent's job is to explain this to him The Plymouth doctors, she admitted with modest satisfaction now know that if they want a nurse to visit someone in the morning they must telephone before 8.30 A.M. and if they want her to visit in the evening they must telephone before 4 30 P.M. while if they wish to talk about a patient they know they can catch the nurse who attended him between 2 and 4 P.M. The nurses for their part carry with them lists showing the surgery hours of all doctors their telephone numbers and their half-days off, so that they can easily consult a patient's doctor when necessary The result of this collaboration is that a nurse (or a doctor) usually comes into the patient's room saying "Doctor (or nurse) has told me all about you"—a reassuring opening letting the patient know that he is in the care of a team Like Dr Barber she has found it more difficult to establish links with the hospital: but the same principles are applied there She explains the nurse's work to the hospital and she interprets instructions from the hospital in such a way that a discharged patient gets continuity of care from the moment he reaches home These are not always easy things to do as some of her examples showed

Thus it is now customary for district nurses to prepare patients for barium meal examinations At one time such patients were expected to report at the radiological department at 10 A.M. after preparation. Miss Williams explained to the department that it is not possible for the nurse to complete the preparation by this time she always has to begin her day by giving her diabetic patients their injections The department now arranges for barium meal patients to attend at 11.30 A.M. Another difficulty arises when a patient needing very large dressings is discharged in the evening or on a Saturday night when it is difficult for the doctor to prescribe what dressings are needed in time for them to be collected before the chemists close—perhaps for the weekend This, too was explained to the hospital and patients needing large dressings are now discharged with a quantity in a Cellophane packing sufficient to tide them over until more can be prescribed

Patients leaving hospital nowadays need far more nursing than they used to do and hence are much more likely to become alarmed if there is any break in care If they are on some drug such as digitalis, an interruption in treatment may be harmful Diabetics are taught in the ward to give themselves insulin, but when they get home everything looks different they lose their nerve, and there may be hours of delay before they get in touch with the district nurse She suggested that *before* any patient is discharged his doctor should be telephoned so that necessary drugs or dressings can be procured the district nurse can be asked to call, and his care can continue without a break from the moment he leaves hospital

The conference demonstrated again the truism that the National Health Service runs not on rules but on people—people willing to take trouble, get in touch explain and understand Such willingness is displayed by and large throughout the country by most district nurses and many general practitioners but not as yet very freely by hospitals Any member of the team, by keeping aloof can hamper the work of the others and unfortunately the brunt falls on the person least fit to take it.

PULMONARY TUBERCULOUS LESIONS

INTEREST in the pathology of pulmonary tuberculosis has been strongly reawakened by the introduction of chemotherapeutic agents which modify the course of the disease and have extended the use of surgery One of the most industrious workers in this field Dr E M. Medlar, of New York has collected his principal findings over the past twenty five years[1]

Before concentrating on experimental tuberculosis and thereafter on the pathology of pulmonary lesions Medlar had already shown himself capable of painstaking work on a very large scale By examining 100 000 *serial sections of* kidneys from 30 cases of pulmonary tuberculosis with caseation[2] he showed that tuberculosis of the kidneys could heal (in 5 of the cases there were healed scars only) and that renal tuberculosis could exist without organisms appearing in the urine and he concluded that "excretory bacilluria" was *invariably* associated with ulcerative tuberculous lesions in the kidney In this work he laid the *foundation* of our knowledge that fundamentally renal tuberculosis is bilateral though it is not always clinically so

Medlar now summarises earlier work which has contributed to the acceptance of new ideas about pulmonary tuberculosis In careful post mortem examinations of 1332 cases of sudden and unexpected death he found evidence of tuberculosis in 1000 though in 785 the lesions were too small to be clinically or radiographically recognisable He found that six-sevenths of the primary complexes were completely calcified Medlar remarks that multiple minute initial lesions in the lower portions of pulmonary lobes seldom give rise to progressive disease but such lesions must be examined to get a complete picture of the disease Only one eighth of these minute healed initial lesions were in the so-called "vulnerable portions" (the apical and posterior parts of the posterior segments of the upper lobes and the superior segments of the lower and right middle lobes) whereas in 96 cases with *minimal* (but probably clinically recognisable) *progressive disease* the great majority of the lesions were in the vulnerable portions Medlar and Sasano[3] who were the first to tackle this problem experimentally showed, by maintaining infected rabbits in an upright position for eight to ten hours each day, that posture was a factor in making some parts of the lung more vulnerable to tuberculosis than others, though the point was not pursued further[4] In the cases with completely calcified pulmonary primary complexes, Medlar found 10% with evidence of reinfection He also found that in 17 of 100 cases of known pulmonary tuberculosis in adults the healing of a primary infection must have been followed by true reinfection behaving like a second primary infection[5] Of the 100 patients 34, aged 16–64, had died as a direct result of primary tuberculosis[6], and from these and the 1000 sudden deaths he concludes that progressive primary pulmonary tuberculosis accounts for the majority of clinical cases in patients less than 40 years of age, while progressive disease from reinfection accounts for the majority of cases in patients over 40 years of age Medlar adds his authority to the belief that smooth apical scars are unrelated to tuberculosis[7]

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[1] Medlar E M *Amer Rev Tuberc* 1955 71 no 3 part 2
[2] *Amer J Path.* 1926 2 101
[3] Medlar E M, Sasano K T *Amer Rev Tuberc* 1936 34 456

Medlar interprets the lesions of human pulmonary tuberculosis strictly in terms of his findings in rabbits He discards his earlier findings in guineapigs,[8] since the lesions there were of the abscess type which did not proceed to complete necrosis Now, in the light of a time sequence evolved from experimental lesions in rabbits some of which were vaccinated with B C G, the lesions in man take the following pattern The initial lesion is a minute area of lobular pneumonia in which neutrophils are the predominant cellular element, but monocytes are also present When the parasites are easily destroyed this lesion heals by resolution If the parasites are less easily destroyed an epithelioid mass forms, and, though it may long persist, it never enlarges and it eventually heals by scar formation Where the parasites reproduce in the initial lesion, necrosis occurs with lysis of many of the bacilli if all are killed, the lesion heals by calcification and fibrosis, if not all are killed, viable bacilli are carried along with the slough to new areas of lung parenchyma and the whole process is repeated, thus producing the complex lesions eventually found by the pathologist Liquefaction of the necrotic material depends on subsequent infiltration by neutrophils and must occur before sloughing In this description hypersensitivity to tuberculin is of little account (Rich[9] goes to the other extreme by implicating hypersensitivity as a most important factor in the degree of reaction) Thus Medlar minimises the importance of tuberculous granulation tissue and the monocyte epithelioid cells, while he emphasises the presence of polymorphs and the occurrence of necrosis Dissemination by the bloodstream is rare (apart from miliary tuberculosis), and by the lymphatics it is relatively innocuous, local expansion does not occur Dissemination is nearly always by way of the bronchi Medlar's illustrations are all at low magnification (× 1 5 to × 15) and details cannot be seen, different elements have to be distinguished by legend descriptions with references to rather indistinct colours This part of the monograph is unnatural and forced, and, with the repeated insistence on the time sequence, monotonous Those who do not wish to exert their own critical faculties should refer to the excellent description of the histological features by Florey,[10] who has himself done much work on this aspect and has inspired much from others Medlar's interpretation of cavity formation in man is also fitted to the development of cavities in vaccinated rabbits or in unvaccinated rabbits inoculated with few bacilli of low virulence the histological description is biased in the same way as that of the minimal lesions (Other recent discus of this topic include those by Pagel[11] and Clegg Despite this criticism of Medlar's interpretation of th structural changes, there is general agreement u his conclusion about the effects of streptomycin p aminosalicylic acid there is no morphological evidence that chemotherapy significantly affects a necrotic le once it has formed, though the non necrotic com (? perifocal reaction) vanishes more rapidly than in days before chemotherapy

RAYNAUD'S PHENOMENON

ALTHOUGH Raynaud's phenomenon is a comm complaint, in only a small proportion of people is th disability severe enough to bring them to the doct The majority of those so examined are in the idiopath group The attacks begin in adolescence and are pre cipitated by exposure of the hands or body to cold Although the recurrent colour changes, cold ache, tingling may be a nuisance, nutritional changes do develop Sometimes the Raynaud's phenomena ma come on in adult life and a detailed search must then made for the cause The digital arteries, whose abnorm response to cooling is incriminated in this condition, ma be attacked by many different lesions The chan in their behaviour is sometimes associated with organic narrowing or occlusion of the vessels, while some the colour phenomena can be more satisfactori attributed to an exaggerated response by the arteri muscle rather than to any narrowing of the lum More rarely, the occlusion of a large proximal arter such as the subclavian, may be the cause The dist between the occlusive and non occlusive groups ca be made quite simply by means of a reactive hypere test or, with great precision, by angiography

The ætiology of Raynaud's phenomena appearing in adult life is less easy to determine The persistent use of vibratory tools is one possibility which is usuall suggested by the patient's occupation Agate and Druett[14] have shown that a frequency of about 40 to 125 cycles per second is required to cause white finger In young men below 35, thrombo angiitis obliterans is the commonest underlying lesion Identical arteri changes are often present in the legs, and a history of attacks of phlebitis is common In some, the disease strikes with dreadful speed, and all four limbs may be lost in a short time, in others, the attacks of angiitis are widely spaced and the lesions small and isolated In older men atherosclerosis, which often picks out isolated digits, thereby giving asymmetrical Raynaud's phenomenon, is usually responsible Lynn et al[15] have lately suggested that "thrombotic digital artery disease" would be a better term when there are local nutritional changes and arteriographic evidence of obliteration of the digital arteries

In women thrombo angiitis obliterans is virtually unknown, although atherosclerotic digital lesions occasionally lead to Raynaud's phenomena Frequently, however, the white fingers make their appearance between the ages of 20 and 50 In such patients a careful physical examination may reveal other skin or vessel lesions, such as scleroderma, acrosclerosis, or disseminated lupus erythematosus, and in these the white fingers are only a minor part of the general systemic affection These diseases account for only a few cases, and many of the others will be found to have joint lesions, flexor tendon nodules, or a persistently raised erythrocyte sediment n rate suggesting a rheumatoid condition The onset Raynaud's phenomenon may indeed precede clinical ns of rheumatoid arthritis by many years, and the e diagnosis is apparent only after a long follow up r the remainder of these women no cause can be found the Raynaud's phenomenon which may or may not associated with structural changes in the calibre of the ssels The severity of the symptoms varies and some nes nutritional lesions or calcinosis circumscripta may use a good deal of distress Barnett[16] in a review of ite fingers due to occlusive digital lesions has pointed t the difficulties of differential diagnosis and emphasised at although a sympathectomy may relieve symptoms does *nothing to alter the march of the underlying* ocess.

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[4] See *Lancet* 1954, ii, 1059, *Ibid* Jan 8, 1955 p 89
[5] See also Terplan, K *Amer Rev Tuberc* 1940 **42** supplement
[6] See also Ustev, H J *Brit J Tuberc* 1946 **40**, 85
[7] See Dawson J Susman W *J Path Bact* 1937, **45**, 597, Dawson J *Ibid*, 1939 **49** 483
[8] *Amer J Path* 1926 **2** 275 291
[9] Rich, A R. *The Pathogenesis of Tuberculosis*, Springfield Ill, 1951, p 368
[10] Lectures on General Pathology London, 1954, pp 623–666
[11] Pagel W *In* Pagel W, Simmonds F A H, Macdonald
Pulmonary Tuberculosis London 1953
[12] Clegg J W *In* Sellors T H Livingstone J L Moder
Practice in Tuberculosis London 1952, p 78
[13] See *Lancet*, March 19 1955, p 599
[14] Agate J N Druett, H A. *Brit J industr Med* 1947, **6**, 1
[15] Lynn R B, Steiner R E Van Wyk, F A K. *Lan*
March 5 1955, p 471

DRUGS IN THE TREATMENT OF DEPRESSION

For the treatment of depression the value of the phetamine group of drugs is now established though st psychiatrists would regard them as ancillary to her modes of treatment Amphetamine itself has been rgely superseded by dexamphetamine sulphate which s *less side-effects and produces less tension, or by* ethylamphetamine hydrochloride These drugs are eful especially during the convalescent phase of a pressive illness in which a patient who has been treated y electroplexy has reached a plateau in his improvement hey are also valuable in mild depressive attacks, articularly perhaps in those of pyknic or athletic habitus nd especially when these reactions are the result of vironmental trauma Rudolf[17] has lately described e treatment of depression—mostly it seems of the lder type—with methylamphetamine in very large oses, which he has found as effective as electroplexy his has certainly not been the usual experience but ssibly few have employed the dosage given by udolf

In using amphetamines it has often been found that nprovement as regards depression was outweighed by an crease in the *associated anxiety and accordingly it* customary to buffer these drugs with short-acting arbiturates such as sodium amylobarbitone A number proprietary products embody this combination in single tablet or capsule Sodium amylobarbitone y itself is also widely used It often produces some uphoria but, even without this, the abatement of ension is encouraging to the sufferer from a depressive llness Moreover it acts and is excreted quickly which makes it less dangerous to the patient who may take n overdose. On the other *hand neither a barbiturate* or an amphetamine drug should be prescribed for any onsiderable period without carefully weighing the risk f inducing an addiction which can easily prove more ntractable and more dangerous than the original disorder[18]

The claims made for chlorpromazine have not all been confirmed by English workers but there is general greement about the value of this drug in treating ension Increasing experience suggests that its chief value lies in its use in association with other sedatives. When *given with sodium amylobarbitone it will often* give rise to tranquillity without clouding of consciousness Such a combination is particularly valuable in the treatment of outpatients or when dealing with severe depressions under general hospital conditions for if the patient can be relieved of unbearable tension the risk of suicide is small Against this as we lately pointed out,[19] is the fact that the drug is by no means always harmless and in some series has caused jaundice in something like 4% of cases As its ill effects are usually heralded by pyrexia the risks are diminished if patients are instructed to stop taking the drug if the temperature rises Pyrexia is seen probably in less than 10% of patients[20,21] but this figure is large enough to compel caution in the use of the drug for outpatients, and especially where there is any suggestion of liver dysfunction as in those older alcoholics in whom depressive illnesses develop Postural hypotension can be avoided by building up the dose slowly and cautioning the patient against exceptional physical stresses while chlorpromazine is being taken

CEREBRAL THROMBOSIS IN THE YOUNG

When a young adult has an unexpected stroke it is proper to search diligently for such causes as tumour, congenital vascular abnormalities, blood disease, embolic disorders syphilis, and polyarteritis nodosa Where no such disorder is found the cause is usually premature vascular degeneration The possibility of cerebral arteriosclerosis may be *overlooked in patients who are* not yet middle-aged Yet Irish,[22] in a review of 1000 necropsies on cases of cerebrovascular disease, reported 17 instances of cerebral thrombosis in patients aged less than 40; and of 30 patients with internal carotid thrombosis described by Gurdjian and Webster[23] 7 were under 40 Berlin et al[24] have now described 13 cases of cerebral vascular accidents in young patients, none was hypertensive, obese or diabetic, and in none did careful investigation reveal any reason for the accident except presumed arteriosclerosis The 1 death was of a patient aged 28 necropsy showed atheromatous narrowing and thrombosis of the basilar artery In a fairly short period of follow up there have been 2 non fatal recurrences

White[25] estimates that of all cases of myocardial infarction about 4% arise in patients under 40 years of age, owing to atheromatous coronary *thrombosis* Atheromatous cerebral thrombosis in youth seems to be little less common

EPSOM COLLEGE

Last year the many friends of Epsom College heard with concern of the school's difficulties and the uncertainty of its future Among the first to respond to the appeal sent out six months ago[26] was the Queen and on May 13 she again showed her interest in the college's welfare by going to Epsom to see the boys at work The headmaster Mr H W F Franklin showed the Queen and the Duke of Edinburgh a good deal of the buildings and grounds and those who use them and there was tea with the *prefects afterwards.*

The first hundred Epsomians assembled on Oct 10 1855 under the eye of the Rev Robinson Thornton the first headmaster and last week's Royal visit was a part of the centenary celebrations The story of these hundred years and the names of those who figured in it have been pleasantly set out in *Epsom College Register 1855–1954*[27] *another important* contribution to the marking of the anniversary But if things are to go on in the same effective way the school and the Royal Medical Foundation of Epsom College must have all the help *they asked for* in their appeal—and that was £150 000 The treasurer of the college is Dr Henry Robinson and his address is Epsom College Surrey

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[16] Barnett A J *Med J Aust* 1955 i 45

[17] Rudolf G de M *Practitioner* 1955 174 180

[18] Hunter R A Greenberg H P *Lancet* 1954 ii, 58

[19] *Ibid* April 16 1955 p 806

[20] Trethowan, W H Scott P A L *Ibid* p 781

[21] Garmany G May A R Folkson A *Brit med J* 1954 ii 439

[22] Irish, C W *J Pediat* 1930 15 81

[23] Gurdjian E S Webster J E *J Amer med Ass* 1953, 151 641

[24] Berlin L Tumarkin B Martin, H L *New Engl J Med.* 1955 252, 16

[25] White P D *Heart Disease* New York 1947

[26] See *Lancet* 1954 ii, 1116

[27] Epsom College Register 1855–1954 Edited by T R Thomson Oxford 1955 Pp 670 Printed at the Oxford University Press for the Old Epsomian Club.

Special Articles

A MAN-CARRYING CENTRIFUGE

Opportunities for Extensive Research

At the R A F Institute of Aviation Medicine at Farnborough in Hampshire a new man-carrying centrifuge has been installed This is a development of great significance to aviation medicine in this country, for the centrifuge has enormous research possibilities The opening ceremony was performed on May 17 by Lord Thurso, formerly Sir Archibald Sinclair and Secretary of State for Air from 1940 to 1945

THE NEED FOR A CENTRIFUGE

The fact that pilots in fast aircraft may " black out " in tight turns has been known since the Schneider Trophy races of 1929, when aeroplanes flew at 350 m p h over a closed circuit It was immediately realised that this was a sign of retinal and cerebral anæmia produced by pooling of blood in the abdomen and legs, for which the centrifugal force was responsible With the mass *production of fast fighter aircraft these physiological* effects became an important hazard to pilots manœuvring at high speed, but little immediate research could be done because any investigation in a flying aircraft was difficult to perform, limited in scope, and indeed dangerous To reproduce the effects under laboratory conditions a centrifuge was necessary, and during the late war centrifuges were built in Canada and the United States, but it was impracticable at that time to build one in this country After the war plans were considered, and by 1947 the main features were agreed upon The apparatus was completed this year and the advances in design incorporated in it are a tribute to the skill and ingenuity of those who made it (M B Wild & Co and General Electric Co) and to the staff of the institute at Farnborough It is the most modern centrifuge in Europe and in some respects, such as the electronic recording, it is the finest in the world It has cost in all about £350,000

CONDITIONS OF OPERATION

Two subjects carried in observation cars, or gondolas, can be swung around a circle of 30 ft radius (fig 1)

The arm carrying these gondolas is 62½ ft long and 9½ ft square in cross section, and it is made of an open lattice work of tubular steel and light alloy It is pivoted on a central vertical pillar The mass to be rotated weighs 42 tons this is set in motion by a D C electric motor which de- 2200 H P

The maximum speed of rotation is 54 4 revolutions per minute, when the gondolas are travelling at 115 m.p.h. The speed can be reached in 9 seconds from rest The radial acceleration is then 30 times the force of the earth's gravitational field—i e , 30 g An acceleration of 5 g can be reached in 1 5 sec This means that the gondolas, which weigh 1150 lb (rather more than ½ ton) at rest, can reach an effective weight of over 15 tons These very high speeds will be used only for testing structures, and it is not proposed to

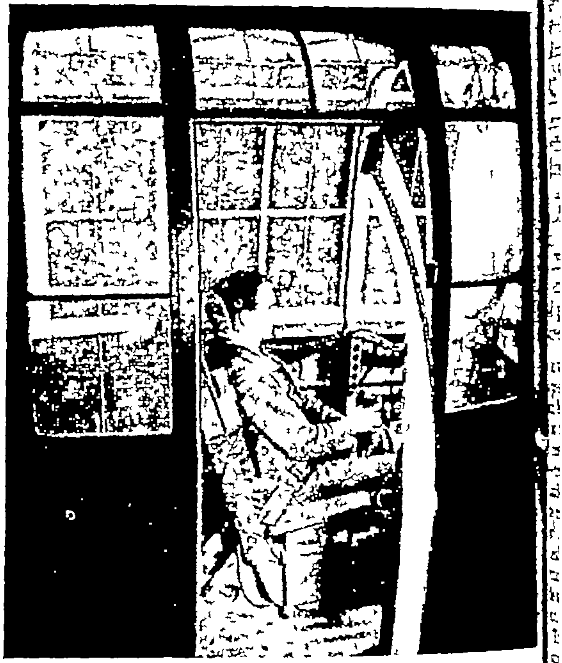

Fig 2—The cockpit of a gondola.

subject men to greater accelerations than 10 g (or possibly 15 g in the prone or supine position)

The gondola is fitted out as a cockpit (fig 2) and is *suspended on a pair of gimbals fore and aft* so that it tilts when it is being rotated The operation of the machine is in the hands of a controller who has an observation room looking into the centrifuge chamber Rotation may be automatically controlled by pre set cams, which determine the rate of acceleration to maximum speed and the time for which it is maintained. A joystick in the cockpit can also be used to alter the speed, but the man in the observation room does most of the regulation

An observer sits in a cabin on the rotating arm close to the axis and watches the subject continuously through the ' Perspex ' upper shell of the gondola, and the physiological measurements are recorded in a laboratory on the floor above the centrifuge chamber

All four members of the operating team—subject, observer, controller, and recorder—are linked by microphone and loudspeaker The subject's reports are constantly heard by all the others, but comments about him passed between, say, observer and recorder, can be kept from him lest they have an undesired psychological effect

PHYSIOLOGICAL INVESTIGATIONS

The centrifugal force required to cause black-out varies not only from pilot to pilot, but also from day to

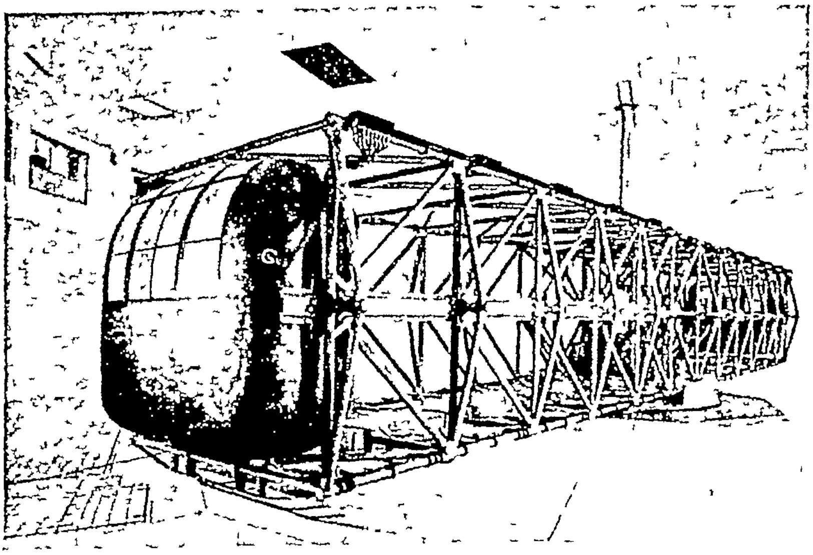

Fig I—The centrifuge chamber

y in the same man Few men can sustain a force of re than 5 g unaided and some will black out at 3–3 5 g hen wearing an ' anti gravity suit, which compresses e abdomen and legs and so limits the pooling of blood these regions, most pilots can sustain forces up to 6 g vertheless at one demonstration an experienced bject unexpectedly started to black out at 5 g even ough wearing a suit Apart from the effect on vision d consciousness the increased weight of the body akes speech difficult and the movement of the limbs mbersome

The measurement of the physiological variables eded to analyse these effects in a subject travelling at) m.p.h is difficult and their recording a major problem ll recording is done electrically and the signals carried leads along the arm of the centrifuge into the central llar They are then led out in the floor above by an genious system of slip rings in a column above the ntrifuge chamber To include the telecommunication rcuits there are 60 silver sliprings each with 2 silver rbon brushes leading to 30 mercury troughs each with spade type collector When it is remembered that .E.G and E C.G signals with a maximum strength of millivolt are led some 50–60 ft through this slip ring stem, the size of the technical difficulties in screening d protecting the signals from distortion will be ppreciated

In the recording room a 12-channel inkwriter (Ediswan) is present in use but a 24-channel photographic recorder will on be available The use to which these channels are put at the discretion of the experimenters. As an example one demonstration it was possible to record from 2 E.E.G ectrodes and 3 E.C.G chest leads. Then an estimate of head lood-flow was made by recording the opacity of the lobe of e right ear photo-electrically and also the pulsation of the rlobe Pulse-rate was recorded in two ways as a continuous ariable and periodically as an integrated count. The maining 8 channels recorded the acceleration of the subject e angle of tilt of the car and the pressure in the anti-gravity uit.

The arterial blood pressure is normally recorded by a apacitance manometer through an intra arterial cannula. he manometer and all the amplifiers are supplied by Southern nstruments Ltd.

In addition there is a cine-camera in the cockpit so that the ubject s reactions may be photographed at any time This enforces the clinical observations of the observer and also the ubjective account of his sensations given by the pilot through is microphone It is planned to include cino-radiographic ecording of heart and lung changes later on

OTHER USES

This standard use of the centrifuge for physiological esearch is by no means its only possibility The gondolas ay be suspended at 10 15, 20, or 25 feet from the centre s well as the end position of 30 feet By this means the ngular velocity component can be varied independently of the total centrifugal force by altering the radius The radial force = ω^2r where ω is the angular velocity nd r the radius of the rotation) As yet little is known of the effect of angular movement per se.

Moreover the gondolas may be replaced by a box like structure of the same dimensions as the cross-section of the rotating arm This is lined with foam rubber so that men may be allowed to move freely in a greatly increased gravitational field This is of particular value in training pilots to don parachutes or get through escape hatches under these conditions which are unfamiliar because of the great increase in body weight The rotating arm may also be used to subject structural devices to great centrifugal forces.

Thus, although the main purpose of the new centrifuge is to extend the research programme of the Institute of Aviation Medicine it will also be of value in training pilots and in testing their fitness to face this hazard of high-speed flying

HEALTH SERVICES OF NORTHERN IRELAND

LAST year the health services were severely criticised in debates in both houses of the Northern Ireland parliament Parliamentary control over the services was said to be ineffective and too much power was in the hands of nominated bodies , lack of coördination, extravagance, and administrative inefficiency were other criticisms made The minister of health in response to these strictures set up a committee under the chairmanship of Mr H G Tanner chairman of the South Western Regional Hospital Board [1]

In its report [2] which was issued last week the committee points out that the ministry of health and local government unlike its counterparts in England and Scotland, is not empowered to provide health services but only to secure their provision by others Thus hospital and specialist services in Northern Ireland are provided not by the ministry but by the hospitals authority and the tuberculosis authority which also provides ancillary services, notably bacteriological and blood transfusion services

Hospital Services

On the whole the committee found that the system had worked well The hospitals authority had shown itself energetic and enterprising Charges of irresponsibility and extravagance were unfounded It had been able to spend more money on capital developments with more freedom than the English regional hospital boards, and from 1948 to 1953 it had increased the number of beds by 10% But the committee considered that the authority's relationship with the ministry was anomalous and should be changed that its internal administration was cumbrous and that it had not always secured the full coöperation of hospital management committees The committee would not wish to see the authority stripped of its executive functions and turned into an advisory body But it recommends that the authority should become an agent of the ministry, for it considers it anomalous that final responsibility for expenditure should rest with the ministry and responsibility for the policy which largely determines expenditure with the authority

> In our opinion responsibility at the highest level for finance and policy must rest with the Ministry We subscribe to the principle that a service which is financed entirely from voted moneys must be subject finally to Parliamentary and therefore to Ministerial, control and we see no alternative to this which does not infringe constitutional practice and precedent and contain inherent possibilities of friction and confusion. If this recommendation is accepted it will establish an unbroken chain of responsibility from Parliament through the Minister and her Department to the Hospitals Authority and the Hospital Management Committees. The essential point is not that the Authority s present powers should be curtailed, but that it should exercise those powers under and on behalf of the Ministry rather than in its own right

The committee also recommends that the members of the authority should be reduced to 20 or at the most 24 ; that not more than a quarter of the members, excluding the chairman and vice-chairman, should be doctors or dentists that the term of office should be reduced from 5 to 3 years and that the basis of membership should be broadened and the committee system simplified The grouping of hospitals, it proposes, should be reconsidered with a view to reducing the number of hospital management committees A more equitable distribution of general endowments would help to establish an integrated service

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[1] The other members of the committee were : Sir George Henderson and Mr J V H Mills LL.D.; Dr G C Kelly and Mr N Dugdale were joint secretaries

[2] Report of the Committee on the Health Services in Northern Ireland Cmd 334 Belfast : H.M. Stationery Office 1955 Pp 86 3s.

The committee suggests that distinction awards should not be made by the authority, but should be granted in Northern Ireland either by a single committee, with jurisdiction over the whole of the United Kingdom, to which Northern Ireland advisers should be attached, or by a committee appointed by the minister of health and local government

Tuberculosis Services

The tuberculosis authority, the committee proposes, should also become an agent of the ministry, with the majority of its members appointed by the minister and not as at present by local authorities A system of retirement by rotation should be introduced When the authority was appointed tuberculosis was a serious problem in Northern Ireland, and the authority has an impressive record of achievement Its success tends to diminish the need for its separate existence, but the committee believes that it still has useful work before it A substantial proportion of the tuberculosis beds are provided by the hospitals authority, and the committee is concerned about the possible ill effects of a prolonged separation of tuberculosis from general medicine Savings in operating and administrative costs should accrue from the amalgamation of the two bodies, and the committee believes that it would be in the best interests of the patients to treat tuberculosis not in hospitals set aside exclusively for that purpose, but in annexes of general hospitals In its view the functions of the tuberculosis authority in providing hospital services might be transferred to the hospitals authority within a period of, say, five years The committee was undecided whether clinic and domiciliary services should be vested in the hospitals authority or in health and welfare authorities

General Practice

The committee considers that the general health services board should become an agent of the ministry, that the term of office of members should be reduced from 5 to 3 years, that a third of the members should retire each year, and that a larger proportion should be lay members It recommends that the board should take over the administration of supplementary eye services from the hospitals authority

The board controls the admission of doctors to its medical list, and the committee agrees that the present control of entry into general practice should be continued for several years "*Its abandonment in present circumstances would undoubtedly lead to a renewal of competition from which none would gain in the long run*" But the committee regards control as by no means a desirable long term solution, and recommends that there should be a survey "directed towards the ascertainment of the conditions and quality of general practice"

ELECTION CANDIDATES

THE lists of candidates include the names of the following medical men and women

LONDON BOROUGHS

Bermondsey—Catherine Orr Ewing, M.B Lond (C)
Poplar—G F Vaughan, M.B Lond (C)

PROVINCES

Barking—* Somerville Hastings, F.R C.S (Lab)
Batley and Morley—* A. D D Broughton, M B Camb (Lab)
Buckingham—D G Evans, M D Lond (Lab)
Carlisle—D McIntosh Johnson, M.B Camb (C)
Gosport and Fareham—* R F B Bennett, B M Oxfd (C)
Hendon—Bernard Homa, M.R C S (Lab)
Loughborough—J D Cronin, F.R C S (Lab)
Louth—D R L M Poirier, M R C S (Lab)
Luton—* Charles Hill, P C, M D Camb (L and C)
Ripon—*-Colonel Malcolm Stoddart Scott, O.B.E., M Leeds (C)
Stoke on Trent, Central—* Barnett Stross, M B Leed
Walsall, North—F R Roberts, M B Birm. (L and C)
Warrington—* Edith Summerskill, P C, M R C.S (Lab)
Wells—Max Bresler, M.R C S (Lab)

WALES

Brecon and Radnor—W S Russell Thomas, M.B Camb (

SCOTLAND

Glasgow, Kelvingrove—* Walter Elliot, P C, M C., M.B. Glas (C)
Perth and East Perthshire—R D McIntyre, M.B. Edin (Scot Nat)
Renfrewshire East—J D Mabon, M.B Glasg (Lab and Coöp)

C, Conservative Coöp, Coöperative Lab Labour L, Li
Scot Nat, Scottish National
* A candidate who was a member of the last Parliament

The Wider World

CHINESE MEDICINE

D W JAMES
M B Lond
LECTURER IN ANATOMY, UNIVERSITY COLLEGE, LONDON

China, like India, has two systems of medical prac Side by side with Western scientific medicine exis indigenous system with a history covering many hund of years When the Communist government came power it was faced with a shortage of technicians in fields, and medicine was no exception An imme programme of expansion of medical schools and hospi was begun Graduates from these schools were tra in Western medicine, but the development and investigation of traditional Chinese medicine was also encouraged The Communist attitude is determined by th simple thesis that the experience of hundreds of year likely to contain things of value Their hypothesis not that Chinese medicine is anachronistic, but that its claims are worth investigation, so that anything usef it contains may be incorporated into the body of moder Chinese medical practice

HISTORICAL BACKGROUND

The first known Chinese materia medica is believed t have been written some 5000 years ago by the Emper Shen Nung (an English edition was published in 1911 The remedies it describes include opium, rhubarb, arsenic, and iron Hwang Ti, over 2000 years ago, ma have anticipated the discovery of the circulation of the blood, for, though he offered no experimental veri cation, he wrote "All the blood in the body is under th control of the heart The blood current flows co tinuously in a circle, and never stops" In ancient tim the Chinese practised inoculation against smallpox by insufflating dried scabs from a sufferer into the nos Cretins were fed on sheep's thyroid and in the fir century A D Hua Tu is believed to have used cannabis indica as an anæsthetic

Practitioners of Chinese medicine, like their Europe colleagues until recent times, served an apprentices of four to seven years The apprentice learned h profession from day-to day contact with his master a the routine of practice Though the scheme of instructi was thus ill defined, a system of government examinati and registration has existed for over 2000 years, and practice without registration has been illegal There we private medical schools teaching Chinese medicine i Peking and Shanghai, but after the 1911 revolution the gradually closed down, and between 1911 and 19 there were only eight qualifying examinations i traditional medicine, all held in Shanghai

THE POSITION TODAY

e Chinese government has encouraged a systematic tigation of the remedies and therapeutic methods of tional medicine Dr Wu Chih chung dean of the cal Institute at Senyang (Mukden) who studied at s Hospital and in the United States, described ese medicine as "a *previously neglected mixture of* rience and superstition, from which we are now g to extract and remould what is valuable—and e is a great deal that is of value. Since 1949 a ber of chairs in the history of medicine have been olished, and there is in progress an extensive survey he ancient literature

he Chinese believe that this approach will be of e than historical interest The investigation of itional herbal remedies is not a Communist innova . Many years ago ephedrine was isolated from the *ma huang* preparations of which have been used in a for centuries. But today such investigations are ducted on a large scale and already over 300 pre ptions have been studied on the recommendation of kers studying the old literature Scientists in the ing public health laboratories of the Academia Sinica m to have been led by this study to the isolation of a g giving promising clinical results against both the ebic and the bacillary forms of dysentery and they at present investigating a drug said to be effective inst pulmonary tuberculosis.

t is hoped that a study of the literature of traditional licine may be useful in other ways For example kers in Peking have surveyed methods of sewer struction practised in China from the Han dynasty yards on the ground that materials and methods may rediscovered which will throw no burden on the ited manufacturing resources now available

CHEN CHIU THERAPY

Perhaps the most striking feature of the present day itude to traditional Chinese medicine is the extension l revival of Chen Chiu therapy *Chen* means needling acupuncture, *chiu* means cauterisation or burning ese techniques have been practised from the earliest es and references to acupuncture by early writers gest its employment using stone needles before the covery of metals 700 sites for needling are described a treatise dating from the Sung dynasty and though upuncture was regarded until lately as empirical it was ieved to be of considerable value In treatment by upuncture needles are inserted into the tissues—the mber site and depth of penetration depending on the ease In some diseases the needles are rotated, or a der like herb may be wound round their protruding ds and ignited

In 1951 an experimental Chen Chiu institute was set by the ministry of public health and charged with the estigation of these methods The impetus to these dies came partly from the eclectic attitude to tradi nal medicine already described but perhaps equally portant was the influence of the Pavlovian school in ssia

Russian biological influence in China is considerable d every medical school and research institute now has soundproof Pavlov room The Pavlov school inter ts disease in terms of a disbalance between cerebral citation and inhibition and Pavlov himself used mild rmal stimulation in therapy His theories are held to ovide the necessary scientific basis for Chen Chiu erapy and to remove it from the domain of empiricism upuncture by virtue of its stimulation of the peri heral nervous system is held in China to be the method l choice to restore a disturbed balance between cortical citation and inhibition The Chen Chiu institute has laimed remarkable therapeutic successes in the treatment of such diverse conditions as rheumatism malaria hypertension tuberculosis, and paralysis agitans Figures published by the institute claim 90% cure of 5115 cases of malaria in army units, and 80% successful treatment of 263 cases of hypertension!

The practice of Chinese medicine is not limited to special institutes Some medical schools have departments of traditional medicine and their undergraduates receive instruction in its principles In the Mukden medical school a traditional practitioner holds the rank of assistant professor of internal medicine and has his own department. Chen Chiu practitioners have been absorbed into army and local government organisations, and the institute has trained 1400 of them since its inception in 1951

It seems unlikely that a hospital patient would be denied the resources of Western medicine if he seemed to need them, for Chinese medicine is regarded as con tributing to scientific medicine not as something which renders it unnecessary The 11th People s Hospital in Shanghai opened in 1954 and devoted to traditional practice, has the services of a consulting staff trained in Western techniques who confer with the traditional practitioners both to establish a diagnosis and to supervise treatment when necessary Bacteriological and radiological facilities are available But in the rural areas a traditional practitioner is often the only doctor

CONCLUSION

Though the Chinese clearly have a strong emotional attachment to a system of medicine which is so much a part of their history this attachment is unlikely to blind them to the results of scientific assessment of traditional techniques. Chen Chiu therapy has received a remarkable impetus as a result of the influence of the Pavlovian school, and it seems probable that for a time at least traditional medicine will colour the main body of Chinese medical practice

My thanks are due to the staff of the 11th People's Hospital Shanghai who supplied much of the information included in this article

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Public Health

School Medical Service

IN his annual report for 1951 Dr C W W Jeremiah, school medical officer for Nottinghamshire refers to the difficulties of attracting young doctors to this work He points out that the shortage of doctors and nurses may give rise to the subterfuge that so much of routine inspection is waste of time—a mere question of rubber stamping the fit. But Dr Jeremiah observes, the value of the routine examination lies in the fact that a child can be evaluated as an individual and not as one of a crowd and he goes on to say

> His early defect can be considered in its proper perspective when the degree of its significance is not determined by the need or otherwise to issue yet another certificate prescription or letter to a consultant The organised methods of routine school inspection are designed to make full investigation and analysis possible even if at times the problem child does upset the time schedule And surely to *know* a child to be free from defect is a matter of no little importance to parents and teachers who have the daily responsibility of its care "

> so long as Medical Officers are required to carry out the functions of this Service it is *not sufficient to say* There is a career in this Service for you. It *must appear* so in the eyes of the young recruit to the profession. It can only appear so if he can see clinical responsibility worthy of his training and conditions of service more nearly approximating to those available to him in other branches of the profession with whose members he has to work in constant association

In England Now

A Running Commentary by Peripatetic Correspondents

THE main object of our journey to Spain has been to sit in the sun and do nothing—except cool off from time to time in the sea—but we had to see the Prado in Madrid, and that alone would have been worth the journey And while we were in Madrid I took time off to visit the department of medicine, run by Professor Jimenez Diaz

At present the department is divided between the University Hospital of San Carlos and the Clínica de la Concepción in the University City, which was opened a month or two ago It is a well-equipped and up-to-date hospital, but what most impressed me was the canteen, designed and decorated by the students of the School of Architecture Light, form, and colour produce a refreshing harmony Over the bar they had put a fresco inspired by Galenical animals, and another is planned of the plants that may produce asthma I wish we sometimes encouraged these fantasies, especially when I think of the "temporary" canteen buildings which disfigure some of our hospitals

We did not get to the canteen until 3 P.M., which is late for lunch even in Madrid, and though my morning had begun only at 10 A.M., everyone else had begun at 9 A.M. The main event of the morning after the ward round was the demonstration of some twenty cases by the senior assistants of Don Carlos and on each he gave his opinion There was some astonishing stuff a lot of hydatid disease, of course, but also a case of cutaneous leishmaniasis from Almería in the South, and other curiosities drawn from gastro-enterology, neurology, thoracic disease, and dermatology Medicine has not yet become fragmented here

The patients, as I saw them on the wards and at this demonstration, seemed to take an intelligent interest in the proceedings There was no attempt to spare their feelings in the discussions of diagnosis and prognosis, even when the import of these was very grave, but they remained unmoved Their attitude was impersonal rather than stoical

* * *

I like plumbers They have the spirit of the craftsman Of course they have much in common with my own profession I watch the plumber doing a lateral anastomosis with fervid admiration. Admittedly, he has certain advantages as a rule he can define and, as it were, seal off his field of operation The vital fluid with which he works may be temporarily cut off There are dangers none the less a mere pinprick in a ball-valve, hardly large enough to admit a staphylococcus, may lead to the destructive overflow of a cistern especially when its catheter is blocked by a bird's nest. It is in diagnosis, however, that our plumber excels Only the other day our hot-water tap in the bathroom became enfeebled to a mere trickle We called in the specialist who in a matter of ten minutes produced from its valve a beautiful specimen of phosphatic calculus

The craft is ancient and rich in tradition I am informed that the lion's head which adorns village standpipes, and used to be seen in elegant Victorian basins, is an offering to Leo under whose benign influence old Nile went into flood and spread its rich load of soil far and wide There are critics who allege that plumbers have not changed their ideas very much during the past two thousand years In houses they tend to festoon their pipes among the rafters—in places accessible only to frost. They have also a passion for what are called "long runs" This means that the kitchen tap has to be turned on for three minutes at least before any hot water deigns to appear But I like plumbers all the same!

* * *

The present epidemic in London is making life unbearable It's bad enough to have to listen in daylight hours to *Tishoo! Tishoo!* but it's infinitely worse to be woken at intervals during the night by a loud *Tishoo!* in the street. What! You haven't noticed it? You must live off a bus-route London Transport buses are being fitted with some new gadget (some kind of jet propulsion?) with the result that every time one of them stops and starts again it sneezes.

* * *

"Tell me," the newly admitted fellow patient cated a stout, motherly body, "is she a doctor,"
"She," I said, "is the Senior Surgeon."

The title was unambiguous enough to impres But his question revealed one of the odder aspects in the wards patients spend hours watching bodies moving before them, but they rarely them correctly Only the orderlies are labelled shoulder flash. Do registrars trembling on the consultantship realise that they are confused with hatched house-surgeons and technicians hunting for the path lab

They may, in a spirit of unconvincing democra that they do not mind, but if the most pote medicines is the doctor himself,[1] should not the know what dose he is taking? What is the effect condition of projecting the same feelings towards all white coats—let alone the first few confusing days he discharges similar quantities of psychic energy to white coats, covering the student, the dietitian, physiotherapist, and the barber? Should not all be labelled?

* * *

I was brought up always to carry two handkerchi one for blow and one for show—and I religiously them every week whether they need it or not Ne theless I feel uncomfortable when I see my fr ostentatiously blow their noses on medicated hy tissues This is not due to any narrow minded that only my ways are right, but to the certain know that I am about to suffer an attack on my personal Your annotation last week on poliomyelitis has com me however You point out that hygienic measures prevented people from getting themselves immunis polio during infancy and have thus converted inf paralysis into the much more serious disease—epi poliomyelitis If these medicated-tissue types get t way we shall find that the ordinary harmless com cold will vanish and its place taken by epidemic co So join with me all you handkerchief men and le fight for the common cold to the last sneeze.

* * *

Seventeen stones of placidity was our Maggie eighteen months she lay abed without a grumble an the end of this time we did a left-sided pneumonect on her You can imagine our pride when a week Maggie's discharge from the sanatorium we picked the local paper to read that it took four policemen hold her down in a drunken brawl

* * *

SONG OF A DEMICENTENARIAN

When I was young I took to my heels,
Danced the lancers and eightsome reels,
Tapped like a metronome, pranced on points,
And never gave a thought to the state of my joints
I was younger, brighter,
And very much lighter,
In those days

When I was young I ate what I got,
Regardless of whether it was fattening or not
I stuffed potatoes and I throve on bread,
And I never gave a thought to middle-aged spread.
I was younger, leggier,
"Bought-it-off the peg" ier
In those days

When I was young I talked very well,
Listened like an angel, and laughed like a bell,
When I felt like clowning I could rock the room,
And I never gave a thought to middle aged gloom.
I was younger, tarter,
And less of a martyr,
In those days

But I'm not dead yet, and presently I
Shall be an old party who'll never say die—
Who rollicks up to London and riots through the sh
And never gives a thought to stopping till she drops
I'll be older, merrier,
And spryer than a terrier,
In those days

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[1] Balint, M. *Lancet*, April 2, 1955, p 683

Letters to the Editor

KWASHIORKOR

R,—

*Me me adsum qui feci in me convertite ferrum
O Doctor Federico Gómez.*

s the earliest importer of the word kwashiorkor" as you, Sir, were the first to perpetrate it in print) d I must defend in your columns its use by my friends, Trowell Dr Davies and Dr Dean

think Dr Gomez (April 30) is mistaken when he ciates malnutrition directly with overpopulation many areas where the disease exists there is no ' keen petition for food ' It often results because the nts do not know what food is suitable for the weaning d. This is admirably illustrated by Autret and Behar[1] uatemala.

r Gomez can rest assured that none of the English ors who are studying malnutrition in African children" any "romantic desire to perpetuate absurd expres of African tribes" What is there absurd ? This l means this disease It is defined as ' the disease child gets when the next baby is born ' And in t countries it has been found that this is indeed the ation often associated with its occurrence It has been fairly extensively investigated and it is proved o largely due to protein malnutrition But possibly is not the whole story Perhaps certain amino s are more important than others Perhaps certain erals, toxic drugs, or herbs will prove to be part of the ure Until we know more accurately what are the ors leading to this disease some people prefer to use word which conveys an idea without yet making ustified claims to detailed knowledge

ertainly other countries can produce whole regiments ames that convey similar ideas As the book referred shows, there are now numbers of generic as well as n names by which the condition or something ilar may be identified

ome of my medical friends were horrified at the word washiorkor" but now many of them have learnt to nounce it quite intelligibly I am sure they will enjoy ming to say "tzipitl

But beri beri is still called beri beri although we now ow it is due to aneurine deficiency Rickets (a word ed probably among primitive Anglo-Saxon tribes) is l called rickets though we now recognise it as amin D deficiency ' Onyalai ' as far as I know has serious rivals. What about ' yaws or even malaria ? ' Kwashiorkor is to some extent a fession of ignorance But I cannot see why because s African it is therefore unacceptable Scipio at any te would not have been surprised

The most puzzling remark in Dr Gomez s letter is when says " It cannot be accepted in the light of modern owledge that there are many types of malnutrition rely one of our main objectives is to identify and stinguish between the many and various types of alnutrition How can nutritional studies advance less we do so ? A case of beri beri a case of rickets case of anaemia each needs its own specific treatment he Ga people recognised a particular form of mal trition They called it ' kwashiorkor

London, W.C.1 CICELY D WILLIAMS

POLIOMYELITIS VACCINE

SIR,—Your American correspondent s report last week p 1018) regarding the Salk vaccine is hardly encouraging may also be pointed out that however dead the irus in the vaccine may be the giving of any kind of oculation is likely to precipitate paralytic poliomyelitis a relatively very small number of children who perhaps re already harbouring the virus One is led to believe that these dangers are less than the benefits of protection but when the protection is by no means 100%, the merits of the method and its statistics become debatable

As your correspondent points out many virologists favour the use of an attenuated live virus given by the mouth This is reported to be effective in provoking the development of antibodies without even causing an abortive illness It is certainly more effective than the Salk method, and may even involve less risk, for should an oral vaccine lead unexpectedly to a febrile illness there are still many chances that no paralytic disease will develop especially if certain precautions are taken When, however, poliomyelitis is precipitated by an inoculation the natural defences of the nervous system seem to be rendered ineffective, and nearly all such illnesses develop into a paralytic form of the disease affecting especially the limb used for the injection

It seems therefore that the oral method can be submitted to clinical trial with as little anxiety as is involved in using the Salk method and many will think that a test of this kind on a considerable scale is not only justified but is urgently called for Should an oral vaccine prove to be safe its administration within the first few months of life might well lead to the disease being conquered "

Department of Neurology,
Radcliffe Infirmary Oxford
W RITCHIE RUSSELL.

STAPHYLOCOCCAL INFECTION IN THE NEWBORN

SIR,—We have read with interest the letter by Dr Court and his colleagues in your issue of May 7 We are at a loss to understand why they have interpreted our article of March 19 as a recommendation that *all* infections in newborn babies in maternity hospitals should be treated *with erythromycin* ' (our italics) It was clearly stated that the object of the work reported was to test the efficacy of erythromycin in *staphylococcal* infection and to determine whether under the strictly controlled conditions of our experiment, erythromycin resistance would develop That it is not our normal practice to treat all cases of staphylococcal infection in the newborn with erythromycin or other systemic antibiotic therapy is evident from the fact that we specifically pointed out that, in most cases of conjunctivitis systemic therapy is not indicated and that we use local therapy in the form of chloramphenicol As conjunctivitis accounts for 60–75% of staphylococcal infection of the newborn systemic antibiotic therapy even if all other staphylococcal infections were treated by this means would be employed only in a minority of cases. We do not however treat trivial skin sepsis with systemic antibiotic therapy provided this clears up during the infant's stay in hospital, but no infant is discharged home with an active staphylococcal lesion of any sort untreated

It appears from the figures they give that Dr Court and his colleagues treat with chemotherapy or antibiotics approximately 75% of all cases of staphylococcal infection of the newborn occurring in their maternity units The proportion of our cases so treated is roughly similar although a little higher They use predominantly sulphacetamide ; we use predominantly chloramphenicol —both synthetic chemical substances both capable of inducing resistance in staphylococci Chloramphenicol however is in our experience the more effective and complete resistance of the staphylococcus to it is less likely to occur Sulphacetamide induces resistance to the other sulphonamides chloramphenicol does not induce cross-resistance to other antibiotics, as far as the staphylococcus is concerned Chloramphenicol [illegible] the advantage that it is unlikely to be used [illegible] therapy

We agree in principle that the use of [illegible] and antibiotic therapy should be [illegible] minimum but we have [illegible] antibiotics fairly extensively in neonatal staphylococcal infection Firstly, we are satisfied that minor staphylococcal infection of the newborn is potentially dangerous and that effective treatment reduces this danger The danger does, of course, extend beyond the period during which the infant is in the maternity unit, and Dr Court and his colleagues do not state for how long their 633 cases of minor infection were followed up

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[1] F.A.O Nutrition Series 1954 no. 13 p 48

A few years ago when we adopted a much more conservative policy than we do now, we became alarmed at the number of infants who had serious staphylococcal infection following minor untreated staphylococcal lesions , and we reported a few of these cases[1] Over the past three years we have not seen serious staphylococcal sepsis develop in a newborn infant who has had minor staphylococcal infection adequately treated , but, to mention only one type of serious staphylococcal sepsis, we have seen in our medical pædiatric wards over the same period 5 cases of staphylococcal pneumonia (1 fatal) in the first month of life following untreated minor staphylococcal sepsis 2 other cases (1 fatal) were probably related similarly to minor sepsis The increased use of antibiotics over this period has not resulted in an increase of antibiotic resistance among staphylococci cultured from random swabs from babies and staff, as the accompanying table shows

STAPHYLOCOCCI RESISTANT TO CHEMOTHERAPY

Year	Sulphonamide	Aureomycin	Chloramphenicol	Penicillin	Streptomycin	Terramycin	Erythromycin
1951		6 %	26 %	88 %	21 %		
1954	23 %	9 %	17 %	85 %	25 %	10 %	

Secondly, we are concerned at the danger of allowing newborn infants with active staphylococcal lesions to return home carrying antibiotic resistant hospital staphylococci Since the incidence of hospital staphylococcal infection of the newborn is so high, infected infants will, on their return home, constitute a considerable reservoir of resistant staphylococci unless steps are taken to control their infection before they leave hospital A recent survey carried out in general practice in Edinburgh showed that 1 in every 3 children under twelve, exhibiting lesions judged clinically to be staphylococcal, was a contact of another case of staphylococcal infection at home The 1000 Families Survey in Newcastle, too, drew attention to the frequent occurrence of staphylococcal cross infection within families Somewhat paradoxically, therefore, rational antibiotic treatment of minor staphylococcal infection of the newborn may actually play a part in limiting the spread of resistant strains to the community

Prevention, not treatment, of neonatal staphylococcal infection must be the ultimate goal, but as yet that appears to be unattainable We have not, as Dr Court and his colleagues suggest, reversed our policy of 1953 We have in fact extended the principle of early treatment of minor staphylococcal infection We should certainly be prepared in the light of new evidence and new knowledge, or a better interpretation of existing knowledge, to modify or change our present practice, but Dr Court and his colleagues have given us no grounds for doing so

J O FORFAR
A F MACCABE
C L BALF
HELEN WRIGHT
J C GOULD

Edinburgh Northern Hospital Group
and University of Edinburgh

PAROXYSMAL MYOGLOBINURIA

SIR,—In their report of a case of paroxysmal myoglobinuria (April 30) Dr Berenbaum and his colleagues suggest the possible existence of an abnormal myoglobin in this disease, and interestingly found normal electromyographic patterns in the affected muscles twelve days after the attack

We have recently investigated a similar case in of 21, in whom the attacks were produced by cold exertion combined Electromyography of the quadriceps before the attack had passed off normal action potentials but of very low voltage μV) It was thought that this low voltage was con with the weakness of the affected muscles and th not significant

Myoglobin from the patient's muscle and examined electrophoretically against pigments from normal human muscle No difference in mobilities over a wide pH range of phosphate was found

Thus our patient showed no electrical abnormality his affected muscles, and normal myoglobin by methods of testing

University College Hospital
Medical School,
London, W C 1

W D FLETCHER
T A J PRANKER

ABUNDANCE AND WANT

SIR,—It would be difficult to find anyone catered for medically than the inhabitant of London, where 254 hospitals run between them, each week, some 2325 outpatient clinics specialising every, or almost every, ailment or illness under the There are 30 devoted, exclusively, to chiropody, hands and fingers, 4 to piles Each year, every is sent a time table,[1] complete with a map, setting detail specialty, location, address, hours for attend and telephone number of all these clinics He can select a competent one for whatever his patient may suffering from and send him there, fully confident he will receive the best expert specialist treatment advice

Of the 2325 clinics, 1000 deal more generally, medicine, surgery, midwifery, pædiatry, diseases of the chest, &c , while 1325 deal specifically with every conceivable condition or illness

Ear, nose, and throat	142
Eye	125
Skin	112
Orthopædic	104
Psychiatric	100
Physical medicine and physiotherapy	84
Teeth	77
Venereal diseases	75
Neurology (including 9 neurosurgery)	66
Diabetes	51
Varicose veins	36
Chiropody	30
Heart (including antenatal heart and 2 E C G)	28
X ray	27
Radiotherapy	26
Genito urinary	25
Rheumatism	22
Sterility	20
Plastic surgery	19
Speech therapy	15
Rectum	13
Geriatric	11
Hearing aids	10
Endocrine	10
Child guidance	9
Hands and fingers	8
Asthma and allergy	6
Special genito urinary (stricture, phimosis circumcision 2 cystoscopy, enuresis)	6
Tonsils and adenoids	5
Parenthood	5

Dietetic medicine
Anæmia
Hæmorrhoids
Massage
Whooping-cough
Tropical diseases
Ultraviolet light
Thyroid
Peptic ulcer
Relaxation
Contraception
Clubfoot
Infectious diseases
Infant welfare
Antenatal (36th week)
Vaccine
Breast
Sigmoidoscopy
Anæsthetics
Remedial gymnastics
Nasal allergy only
Bronchoscopy
Nephritic
Scoliosis
Hot wax baths
Epileptic
Hay fever
Electro-encephalography
Sinus
Juvenile rheumatology
Allergy in children
Resettlement clinic
Babies (feeding and management)
Premature babies

In addition to keeping the citizen fit, the State very naturally, interested in procreation Thus mothers babies, and children are extremely well cared for, addition, there are 20 clinics for sterility or subfertility Coincidently, 75 clinics deal with venereal disease, another 25 with genito-urinary troubles

It pays the State, of course, to tackle venereal disease and all this could not be better organised every lavatory directs the sufferer, man or woman, to est centre where he can have confidential treatment advice.

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[1] Forfar, J O, Balf C L, Elias Jones, T F Edmunds, P N *Brit med J* 1953, ii, 170

[1] Time table of Outpatient Clinics at Hospitals in the Gr London Area From King Edward's Hospital Fund London, 10, Old Jewry E C 2

nfortunately the State like most of us, cares little hose child weep, so his laugh We people who find faction in befriending the alcohol patient are appalled in this city of 8 million people not one of its clinics rs for the alcoholic or his helpless relatives If the were known it would pay the State to befriend ng countless others the man or woman unfortunate ugh to contract alcoholism There are in this country on half a million people suffering, directly or rectly, from its repercussions

t is no good suggesting that these people should apply ne of the many clinics for psychiatric trouble These r of course, what they can but they are not usually pped or inclined to deal effectively with this rewarding complex medical task requiring ' green fingers ' as l as persistence and perseverance Alcohol patients their susceptibilities and diffidences Like the rest ts, they require to know of a place where they will be erstood and not scolded Our modest plea is that ng the 2325 special clinics there should be one oted to their needs

H PULLAR STRECKER
Hon. Secretary,
kworth, Middlesex Society for the Study of Addiction.

A BARBITURATE ANTAGONIST

SIR,—Discussing the failure of ββ methyl-ethyl glutari le (Megimide) to act in a case of phenobarbitone soning recorded by Dr McElligott (April 16), fessor Shaw (May 7) remarks that 'at the end of days there would be little barbiturate in the body is not so Butler et al[1] estimate that the proportion phenobarbitone eliminated from the plasma in the rse of a day lies between 11% and 23% My own ervations suggest that the figure is approximately % per day[2]

pplying the latter figure in this particular case it will en that 27 grains of phenobarbitone would remain in the y six days after an initial dose of 72 grains assuming t for practical purposes, all the barbiturate was absorbed fact owing to the comparatively slow rate of absorption phenobarbitone shown in this case by negative urine ts for barbiturate on the evening of admission, it is very likely that 15% of the full dose was eliminated during the t twenty four hours and therefore the calculated amount aining at the end of six days is an underestimate

The patient is described as obese ; assuming that her ght was between 10 and 15 stone and that her body fluids resented 70% of this weight a conservative estimate of blood phenobarbitone level at the end of the sixth day ld be between 4 0 and 2 5 mg per 100 ml. Blood levels this order are frequently associated with quite severe ptoms of intoxication and sometimes with coma. It is noteworthy that the dose of megimide was administered hours after admission—i.e nearer the end of the fifth n the end of the sixth day in hospital

Admittedly anoxia and shock frequently contribute producing coma which is *disproportionately deep for* blood level, but I doubt whether there is much dence in support of Professor Shaw's further state ent that by this time [six days] however there ould have been extensive cellular damage—e g ebral œdema Were this true it is surprising that on this time she *showed fairly rapid improvement*

So many barbiturate antagonists have enjoyed brief opularity in the last twenty years that it does seem ust important to control new remedies by blood rbiturate levels—particularly since the results of purely servative treatment have been shown to be so good[3,4]

The London Hospital E.1 J T WRIGHT

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[1] Butler T C Mahaffee C Waddell W J J Pharmacol 1954 111 425
[2] Wright J T Quart J Med 1955 24 95
[3] Nilsson E Acta med scand 1951 suppl. no 253
[4] Locket S, Angus J Lancet 1952 i 580

RUPTURE OF LAPAROTOMY WOUNDS

SIR,—Mr Walton (May 7) draws attention to adherence of the prolapsed abdominal contents to the wound edges as a feature of "burst abdomen ' and uses this as evidence for his view that the peritoneum is the most important layer of the abdominal wall My experience differs from his in that in some cases there were no such adhesions in many the adhesion was to the peritoneal edge, and in a few only to the subcutaneous tissue also The later the rupture the greater was the likelihood of such subcutaneous adhesions and in these cases the escape of serous fluid had told of the earlier disruption of the deeper layers The skin sutures, therefore had not been removed in an attempt to avoid a ' burst ' and to leave the patient, temporarily at least with the safer incisional hernia In one case only in the whole series had the skin sutures been removed before the rupture occurred From this point of view skin closure with interrupted mattress sutures was safer than with Michel clips supported with a few sutures, though it did not confer immunity from rupture

It is perfectly true, as Mr Walton states that if the peritoneum remains intact there will be no burst abdomen but there may be an incisional hernia. It is equally true that if the anterior rectus sheath remains intact there will be no burst abdomen ; nor will there be an incisional hernia unless the scar stretches later We have all had the exasperating experience of struggling to close thin peritoneum in an obese patient, when each stitch hole rapidly expands even though to distribute the tension over a wider area all sutures are inserted before pulling any of them tight To me it is inconceivable that in such a case the peritoneal stitch is not torn out by the first postoperative cough or vomit *yet few of these patients disrupt* their wound and if the anterior rectus sheath is sutured carefully to avoid gaps, it is my impression that not all of them develop incisional hernia. Peritoneum is known to regenerate quite rapidly and I believe that if the rectus sheath heals by primary union no great harm results. I suspect, however that this tearing of the peritoneal suture line is a common cause of adhesions to the scar

Mr Walton surely destroys his own case when he says and in all cases I have noticed the firm adherence of part of the prolapsed bowel or omentum to the edges of the peritoneum and the subcutaneous tissue Surely this suggests that some part of the peritoneum has given way at an early stage. Small gut or omentum protrudes and lies just deep to the skin This can occur only if the anterior rectus sheath also has given way We must consider however the possibility of the fascial layer giving way some days after the peritoneal layer If the skin holds still longer this is a ready explanation of Mr Walton's findings and is, I submit the likely explanation of the late group of cases. A well-sutured skin wound, though obviously not consolidated, is quite soundly healed in six or seven days and even allowing for the difference of tissue and of blood supply I think it fair to assume that the rectus sheath still supported by sutures will at this stage withstand some degree of abdominal distension unless there is some factor reducing the rate of healing In the series I described in my article of March 12 such a factor was present in the form of stress hæmatoma, sepsis, or depleted serum protein. Probably there is no sharp dividing line between the early and the late groups—it would be astonishing if there were—but the evidence from the small number of cases described is that in the early cases the rupture is due to the breaking or to the tearing out of sutures and in the late cases to some factor or factors delaying healing

Turning now to the last paragraph of Mr Walton's letter most surgeons including myself have the *impression* that transverse and oblique wounds are less likely to rupture than vertical ones but there are few statistics on this point and those I quoted[1] do not support the view I made no mention of methods of closing the abdomen as so many have been described and I had no evidence to offer of the merits or disadvantages of each but for the past two years I have been using a continuous horizontal mattress suture for both peritoneal and fascial layers with in addition several interrupted horizontal mattress sutures for the latter During this period there has been only one "burst" but this I shall regard as fortuitous only, unless the passage of several years more confirms the reduced incidence Mr Walton's other points agree with those stated or inferred in my paper

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[1] Wolff W I Ann Surg 1950 131 534

Hove A STANDEVEN

RADIOLOGY OF PLACENTA PRÆVIA

SIR,—We note with interest the correspondence which has followed our article of April 16 Our experience of placentography is limited to the past three years, but we have come to rely on the method to show which cases of antepartum hæmorrhage are due to placenta prævia and must therefore remain under observation in hospital In our article we described how radiology has helped in the management of cases of anterior placenta prævia delivered by cæsarean section

An important point yet to be determined, we believe, is the extent to which placentography can replace the final vaginal assessment by the obstetrician in the theatre Mr Percival (April 23) has suggested that there should be no "percervical" examination when clinical and radiological evidence points to a major degree of placenta prævia We appreciate his reasons for wishing to proceed to cæsarean section without delay and would agree that there are certain cases where this action might appear justifiable Nevertheless we consider that there is a need for caution in this matter

Despite the claims of Dr Blair Hartley (April 30) and the great contribution he has made to the radiographic localisation of placenta prævia, we are impressed by the difficulty in establishing by postural and soft tissue radiography the exact extent to which the placenta encroaches on the lower uterine segment It is the difficulty of defining precisely the lower edge of the placenta in many cases of placenta prævia which makes us believe that there is still a place for careful vaginal assessment before the final decision as to vaginal or abdominal delivery is made Without this vaginal assessment it may be difficult to agree upon what constitutes a "major" degree of placenta prævia For the individual patient it is important to avoid an unnecessary cæsarean section, particularly as placenta prævia is not a recurring condition and between 40% and 50% of cases can safely be delivered per vaginam

Even with radiographs of the superb quality produced by St Mary's Hospitals, Manchester, it is only in 30% of pregnant women after the thirty-second week that it has been possible to demonstrate placental calcification Moreover, the demonstration of placental calcification does not necessarily enable the lower edge to be identified, especially in cases of placenta prævia Until it is possible to do this precisely we believe that vaginal examination in the theatre is indicated

J K RUSSELL
C K WARRICK

Royal Victoria Infirmary,
Newcastle upon Tyne

*** In an article in this issue (p 1045) Mr Percival and Dr Murray record their experiences of soft-tissue placentography —ED L

A VISIT TO KOLTUSHI

SIR,—I note Dr Foggitt's criticism last week of my letter of May 7 He makes a serious charge that I show a "doctrinaire disregard of facts" On the contrary, in the last paragraph of my letter, I stated a procedure enabling a person to *demonstrate* a fact disregarded by Pavlov and his followers I refer to the fact that a person who employs a technique of conscious guidance and control of reaction enabling him to guide the manner of the working of the self as a whole by means of the primary control of the use of the self, head forward and up, thereby controls the self in such a way that it may be *demonstrated* to work as a unity

It works, therefore, in a manner preventing the from interfering with the needs which are vital providing the freedom enabling the human ma work in the best possible way as a whole As a con "vital" processes such as digestion, respiration, and work in what may be *shown* to be the best way, and fore, in a way capable of preventing disturbances of function, incidents such as bronchospasm and the thought associated with what is recognised as schi

Freedom of thought and action are essential not "the scientific world" but in the world at large, described a practical procedure whereby a person provide himself with these advantages Dr Foggitt ca this for himself by employing the procedure I set down last letter If he has not enjoyed the experience nece to this end, both Mr F Matthias Alexander and I will be to *demonstrate* and discuss for his benefit the *objectiv* cedure involved If he is prepared to accept this invit he will discover that he will be required to show an unre "meticulous objectivity" in giving his attention to details of the procedure, if he wishes to employ it in a m enabling him to provide for his use a self working at it therefore, in a way associated with kinæsthetic infor about near and distant influences in the environment, external and internal, working in a reliable way, and, t fore, in a way enabling him to prevent himself from dominated by reflexes conditioned by his environment whose influence over him he would otherwise be ma Unless he employs the procedure with a meticulous atte to detail, he may very well find himself enslaved by r controlling his behaviour in a way that makes him in sense free

Bolton Lancs MUNGO DOUGLA

IRON-DEXTRAN COMPLEX IN MICE AND

SIR,—It would be unfortunate if Dr Nissim's ing article (April 2) were to pass without further con than that so aptly made by Dr Golberg and colleagues in their letter of April 16

The title of the paper, the dramatic photom the tenor of the discussion, and the brief concl summate to produce in the mind of the casual read impression that the administration of intramuscular might be followed by the development of testi atrophy in a male patient

We have found that, despite Dr Nissim's reserval at the beginning of his discussion, this impression already been gained by those who have not cal that the same relative dosage in man would in injection of between 30 and 200 times as much as w ever be given clinically, given moreover to patients a deficiency of iron The inference, therefore, that iron compound apparently interferes with the r metabolism of the endocrine cells and upsets sp togenesis" is unreal when applied to clinical m and, is an example of the way in which the acad pharmacologist may become divorced from the realit practical therapeutics

Furthermore, Dr Nissim states loosely that deposition of iron in the testes after the administra of imferon reminds one of the *deposition of iron in testes* [my italics] and testicular atrophy in hæ chromatosis" This statement could be taken to his results in mice with gargantuan doses (doses ma be noted, only possible because the preparation is of toxicity) to those which might be expected in man It moreover, a misstatement of fact as iron depo does not occur in the testes in hæmochromatosis and Sheldon[1] pointed out, the only appreciable iron dete able in the testes is small quantities in the vessels It the experience of Dr Mary K Macdonald in the de ment of pathology, University of Edinburgh, and myself that iron deposition never occurs in the tub or interstitial cells of the testes in hæmochromat and, when the patient is hypogonadal, the testic atrophy is probably secondary to pituitary infiltra on This infiltration which may be very dense o noted by Sheldon and further commented upon bble[2] as the probable explanation of the hypo m of hæmochromatosis. Dr Nissim assures us ren in this type of experimental siderosis no y deposition of iron is found

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[1] Sheldon J H Hæmochromatosis London, 1935.

iron-dextran complex has been shown to be a e therapeutic agent[3-6] and it would be a pity if ysician were deterred from using it because of the nental results reported by Dr Nissim

tment of Therapeutics,
ersity of Edinburgh.

ALASTAIR G MACGREGOR.

CANCER

—Mr Malcolm Donaldson's challenge (May 7) to ychiatrists to join him in the study of the effect er education on the public is most welcome This ign is going through the same phase that marked esigned to give accurate information to the public nereal disease tuberculosis, and insanity Even e subject of these illnesses is in some quarters ched with bated breath One by one following ement, the 'bad objects upon which are ted the inner fears of destruction are being replaced ers

late Dr John Rickman put the position clearly r columns just before the outbreak of the late war he pleaded for the maximum information about the g dangers pointing out that when this was available ividual could summon resources to face the situa ithout evasion During my ten years as a family an, I frequently found that frankness and the of as much verified information as possible led to inution of strain in the doctor patient relationship nt this by bitter experience following the use of n and subterfuge which I rationalised as being the t approach to a suspected or confirmed cancer case

ALFRED TORRIE.

—Until I read the article by Mr Donaldson s in favour of educating the general public, hen a surgeon admits he underwent an explor laparotomy for a non-existent gastric carcinoma auses for thought Surely it is in members e medical and nursing profession and their rts that fear of cancer is most prevalent and most tent If those who are more or less fully educated s subject suffer most it is folly to increase know in the general public In the National Health re any patient with a symptom he cannot himself in will be very likely to consult his doctor but if s a symptom he thinks may be due to cancer he is ly afraid to be told what he fears the truth may be aits till it disappears or gets worse Thus the less verage man or woman knows of the early symptoms ncer, the more likely will they be to seek medical e early This is not very reasonable—but then especially frightened man is not a very reasonable al

dresbury
stan

HAZEL B BAKER.

,—The subtitle The Psychosomatic Disease to Donaldson's article reminded me of a patient in her le seventies who died recently from multiple ndaries from a carcinoma of the colon Her illness been slowly progressive and she had had an opera to relieve the obstructive aspect of it nine months iously On her death bed although she was unaware he diagnosis she was quite certain that she knew when this trouble with which she was dying had originated This she stated quite categorically was seven years ago when the minister of the church, which she had reverently cared for for many years and which she had many times scrubbed on her hands and knees, told her very gruffly to leave and not to come back Thought of this incident grew in her mind until it was all consuming in much the same way and at much the same time as the cancer developed and consumed her body

We know that suggestion can remove at least certain innocent growths on the skin and can cause 'burns' without heat. Is it possible that it can also cause abnormal growths in the body?

In this case I expect my colleagues to agree with me that coincidence and the desire to blame somebody for one's troubles are the most probable explanations—but I would be interested to hear of any similar experiences

Workington

R N R GRANT

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ald C D Lancet 195 i 1123
ard, I M., Todmore D A Ibid 1951 ii 914
pbell D F Hutchison H E, Hendry E. B., Conway H
Brit med J, 1954, ii 1335
nnison, R. I Ellis H R Lancet 1954 ii 1343
tt J M., Goran A D T Brit med J 1954 ii, 1?3

AGAMMAGLOBULINÆMIA

SIR,—In a review of the literature on agammaglobulinæmia Grant and Wallace[1] pointed out that human malnutrition is associated with low gamma globulin levels and suggested that this might cause increased liability to infection Some recent investigations have shown that gamma globulin levels are usually normal in undernutrition[2] and normal or high in malnutrition[3,4]

We have tried to assess antibody production in children suffering from malnutrition (kwashiorkor) For a variety of reasons we were unable to study antibody response resulting from antigenic stimuli such as typhoid vaccine, diphtheria toxoid or other substances commonly employed for this purpose We therefore chose isohæmagglutinin levels as an indication of the ability to produce antibody

Isohæmagglutinin levels were determined in 15 severely malnourished African children aged eight months to three years and in 3 normal controls of the same age-group All titrations were carried out at the same time and on the same test cells The results were as follows:

Malnourished Children

Group	*Anti A titre*	*Anti B*	*Group*	*Anti A titre*	*Anti B*
A		1/16	O	1/16	1/32
A		1/4	O	1/2	1/1
A		1/128	O	1/64	1/128
A		1/16	O	1/16	1/16
A		1/4	O	1/8	1/8
B	1/64		O	1/32	1/32
B	1/8		AB		
B	1/16				

Normal Children

Group	*Anti A titre*	*Anti B*	*Group*	*Anti A titre*	*Anti B*
A		1/32	O	1/16	1/8
A		1/32	O	1/512	1/512
B	1/1				

Gamma globulin levels as determined by paper electrophoresis in the malnourished group were normal or high

With the exception of 1 of the controls in which the titre was much above the average the isohæmagglutinin titres in the malnourished children did not differ significantly from those of the controls or from those usually encountered in this population and therefore did not provide evidence of impairment of antibody production

In the Medical Research Council report[2] it was shown that in undernourished populations antibody production is somewhat impaired but not sufficiently to increase susceptibility to intercurrent diseases

South African Institute for
Medical Research
Johannesburg

Baragwanath Hospital
Johannesburg

A ZOUTENDYK
C G ANDERSON
I KAHN
H STEIN

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1 Grant G H., Wallace, W D Lancet 1954 ii 671
2 Studies of Undernutrition Wuppertal 1946-49 Spec Rep Ser med Res Coun, Lond no 275 London 1951
3 Anderson C G Altmann, A Lancet 1951 i, 203
4 Trowell H C Davies J N P Dean, R F A Kwashiorkor London 1954

UTERINE CIRCULATION IN LATE PREGNANCY

SIR,—Dr Morris and his colleagues (Feb 12) suggest that some trigger mechanism is responsible for the sudden onset of eclampsia The sudden release of cortical and medullary adrenal hormones by histamine or acetylcholine would be one explanation

The primary rôle of adrenocortical hormones in the genesis of œdema is proved by its appearance, as a side effect, during corticotrophin (A C T H) therapy of diseases of very different ætiology In these cases, there is no question of a reflex mechanism, but only of a hyperfunction of the adrenal cortex Clearly, adrenocortical hormones, such as hydrocortisone, are able to pass through the wall of the capillaries and into the cell, drawing with them sodium, serum, and a varying quantity of serum albumin, against the osmotic pressure of the serum proteins

Benzodioxane proved to be unreliable in cases of phæochromocytoma, giving false negative results [1 2] The rise in the blood sugar level, which has been repeatedly confirmed, is best explained by liberation of adrenaline during the preceding attack Macchiarulo [3] demonstrated the presence of adrenaline in the blood after an attack Professor von Euler has told me that this subject has been investigated in New Haven, but so far as I am aware nothing has been published Medullary hormones are elusive, because they are soon destroyed by the mono amino oxydase, in this light, the sudden drop in blood pressure after an attack must be explained, and there is a better chance of demonstrating medullary hormones if blood samples are taken immediately before or during an attack

There is indeed some controversy about the question if the excretion of urinary corticoids is increased during toxæmia, as compared with normal pregnancy The methods now in use are unsatisfactory, and more specific techniques are being developed (by Nelson and Samuels, for example) for hydrocortisone—as many believe, the natural cortical hormone A second objection is that most of the cortical hormones are retained in the cell out of reach of these reactions That the adrenals are in a state of hyperfunction during pregnancy is confirmed by the amount of uropepsinogen excreted in the urine, this is increased in all cases of hypercortism of whatever cause, and during pregnancy [4]

In my opinion, the statistics of Rh incompatibility show that toxæmia does occur in multiparæ The histaminolytic index, although it rises in pregnancy, may be even lower during toxæmia than in normal pregnancy, this makes it more probable that, during toxæmia, histamine may persist if it is produced in large quantities by an allergic reaction In these circumstances histamine will be available to liberate adrenal hormones Lack of histaminase immediately after delivery may account for puerperal eclampsia, and lactation causes renewed adrenocortical hyperfunction By the close relation of cortex to medulla, a vicious circle may easily result

Much work is being done on the influence of the adrenocortical hormones on renal function There is evidence that glomerular filtration is influenced by large quantities of cortical hormones serum albumin passes through the walls of the glomerular capillaries into the tubules, and proteinuria (also a side-effect of corticotrophin) results The renin hypothesis is not generally accepted [1]

Adrenocortical hormones increase sodium loss and reduce œdema in nephrosis by suppressing the existing hyperfunction of the adrenals and causing atrophy of these organs [5] Renal ischæmia may be caused by freshly liberated noradrenaline, which produces generalised vasoconstriction Histamine, or some H-substance, which can be neutralised by antihistamine, is able to do this too, but is at the same time responsible for reducing blood-pressure by capillary dilatation In eclampsia hypertension predominates

Methacholine ('Mecholyl') can also liberate adrenal hormones, and probably acetylcholine too When much acetylcholine is present in the uterine muscles, the capillary walls allow red cells to pass

Neostigmine prevents the hydrolysis of acetylcho- when, in cases of amenorrhœa, neostigmine injec given on two succeeding days, so much acety accumulates in the uterine muscles that uterine not true menstruation, follows

Is it not possible that abnormally large of acetylcholine, the product of some allergic may be responsible for a Couvelaire uterus or haemorrhage, with disturbance of the normally placenta? The appearance of the internal orga closely resemble that found in the Schwartzmann phenomenon

Amsterdam R S

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[1] Fishberg, A M Hypertension and Nephritis 5th ed. London 1954, p 936

[2] Paschkin, K E Rakoff A E, Cantarov A Clinical Endocrinology New York 1954

[3] Macchiarulo O *Arch Gynaeck* 1935 159, 666

[4] Balfour D *Advanc intern. med* 1954, 6 20

[5] *Proc Mayo Clin* 1953 28, 659

REACTION TO VITAMIN B_{12}

SIR,—The anaphylactoid reaction following the tion of refined or crude liver extract is well I have not been able to trace in the literature reaction following vitamin B_{12} injections R however, I have seen a patient who has been vitamin B_{12} injections as well as to injections of or crude liver extracts

Briefly, the patient has suffered from pernicious the past thirteen years She was treated with extracts for eight years and then had a sensitivity after each injection This took the form of a anaphylactoid reaction with urticaria of the skin ment was therefore changed to vitamin B_{12} inj my surprise twelve hours after each injection she precisely the same form of reaction as after extracts This happened on numerous occasions T ment was then changed to an oral preparation of liver ('Pabryn') and no further trouble has been The blood count and hæmoglobin concentration have satisfactory on this treatment

Dudley Road Hospital,
Birmingham R O GILL

PHENYLBUTAZONE AS ANALGESIC

SIR,—Phenylbutazone ('Butazolidin') is a valuable addition to the treatment of like cortisone, it has certain risks Some years use purely as an analgesic was recommended I followed the method ever since and I find that greatly appreciated by patients, whether they rheumatoid arthritis or osteo arthritis One tablet is given night and morning until the pain is but the drug is not given for more than three days total of six tablets does not give relief, then p butazone is useless in that particular case If successful, however, then after a period of anyth a week to a month or longer, whenever the pain the same course may be repeated

Another extremely valuable use for phenylbutazone severe and lasting reaction *follows the injection* of a vaccine Anti rheumatic vaccines are of considerable sometimes, owing to hypersensitivity, they are not even in minimal doses In such cases, a 200 mg table at the *time of the injection*, and another the same will be found to be successful in preventing reaction. T not appear to suppress the euphoria and relief which *follow a suitable dose Of 20 hypersensitive* cases this way over the last two years, none have failed to

This naturally leads one to speculate on the m action of the drug Does it suppress the antigen-a reaction and thus prevent radical cure or perhaps down? I am grateful to Dr W S Stoddart, of Geigy, for sending me a quotation from a recent a Fabre and Berger [1] in which they show that the a antibody activity continues in serum-sensitive treated with phenylbutazone just as well as in the They suggest that the drug in some way reinfo impermeability of the capillaries, quoting the w Franceschetti and Chodos [2] who have reported an ution of capillary permeability, as tested by the ge of fluorescein in the anterior chamber of the eye. low we assume that the manifestations of rheumatic es are at least in part, the result of localised ons to an infective factor, then slowing down the ption of antigen should decrease the reaction caused too sudden combination with the antibody con in the affected cells

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[1] Fabre and Berger *Sem Hôp Paris*, 1955 30, 87

[2] Franceschetti A, Chodos, J *Arch Ophtalmol.* To be

thanks are due to Messrs Geigy for supplying phenyl ode for trial

don, W 1

H WARREN CROWE

VERHYDRATION AND UNDERHYDRATION

k,—Those who are relatively isolated from advances edical thought and knowledge must be very grateful rofessor Bull for his Goulstonian lectures published ur issues of April 9 and 16 For me the lectures vividly clarified the understanding of the basic ology underlying the many diverse conditions ribed

those unfamiliar with the subject (*as I am*) the of the terms ' overhydration and underhydra may, however be a bit confusing When referring intracellular compartment overhydration ' is used cribe an abnormal excess of water relative to total lable osmotic activity of that compartment (that sentially, a state of hypotonicity) whereas this , when applied to the extracellular compartment s to a state of increased volume accompanied by a ortionate increase of total available osmotic activity is, an expansion *without* change in osmotic tension) le no etymological objection can be made to the inology used by Professor Bull, I feel that a slight ge may make the subject clearer for many readers

would suggest that for any fluid compartment, erhydration be absolutely restricted to those s where there is a reduction of the osmotic tension he compartment under discussion—i.e where there excess of water relative to total available osmotic vity Where the reduction of tonicity is due primarily reduction of total available osmotic activity and to an excess of water relative overhydration ht, perhaps be used and where the reduction of city is due primarily to an excess of water absolute rhydration ' might be used Similarly underhydra would be absolutely restricted to those states re there is an increase of the osmotic tension of the partment under discussion If the concept of osmotic librium is accepted—that is to say if it is accepted t there is always either zero osmotic gradient or else a stant unchanging gradient between the fluid com tments—then it must follow that (using this termin gy) an overhydration of one compartment would be ariably accompanied by an equal overhydration in other

y suggested terminology now leaves us without a term to cribe those states classified by Professor Bull under the eral heading of extracellular overhydration and without rm to describe some of those conditions described by him xtracellular underhydration I suggest that when reference being made to changes in the volume of a fluid compartment terms "expansion and contraction should be used ere the expansion or contraction is unaccompanied by a nge in osmotic tension one might if this were necessary clarity refer to iso-osmotic expansion or contraction; re the change of volume is accompanied by a change of motic tension the appropriate prefix hyper-osmotic or po-osmotic might be used or alternatively the words with underhydration or with overhydration" might be ded, preserving the rigid definition of underhydration and ehydration given above

Thus for example severe sodium depletion without restric n of water intake would lead to a state to be described as po-osmotic contraction of the extracellular compartment or extracellular contraction with overhydration—an intra- llular overhydration also of course resulting Sodium pletion with restricted water intake would lead to an iso-osmotic or hyper-osmotic extracellular contraction or alternatively to extracellular contraction without or with underhydration

The advantage of this terminology is that it would pin point more clearly the essential biochemical abnormality and indicate the appropriate treatment as the following examples show

Professor Bull classifies the œdema of congestive heart failure under the general heading of extracellular overhydration This might suggest that the basic abnormality was an excess of water and that the correct treatment consisted in restricting water intake Using the suggested terminology this condition would be referred to not as extracellular overhydration because there is no essential reduction of tonicity but as extracellular expansion The term extracellular expansion would help to emphasise that the œdema could only be corrected by removal from the body of some of the extracellular osmotic framework (or osmotic stuffing as Black aptly describes it [1])—that is, by depleting the body of its excess sodium. The term overhydration (unqualified) would be restricted to those states where there is a simple excess of water throughout the body and where treatment would consist in withholding water and allowing the patient to dry out

The production of extracellular contraction accompanied by intracellular overhydration is a serious risk in modern surgical practice This risk arises from the emphasis at present being laid (quite correctly when conditions are appropriate) on a liberal intake of hypotonic fluids. The condition results when a liberal intake of hypotonic intravenous fluid is begun *before* a severe extracellular contraction has been re-expanded. The circulatory renal insufficiency prevents the water being excreted, renal function may be depressed by the resulting fall in serum sodium and the patient may die from water intoxication If the *condition is* allowed to proceed to an extreme degree the only effective treatment may be administration of hypertonic saline (e g 5% NaCl solution) a fluid which may not always be readily available

It cannot be too strongly emphasised that 5% glucose solution when injudiciously administered at the wrong time to a severely salt-depleted patient is a potentially lethal fluid During the past year I have seen several surgical patients who have been on routine intravenous fluid therapy for some time with serum sodium levels below 130 m.eq per litre While several factors have doubtless contributed to the production of these hypotonic states (e g , early postoperative water retention [2] severe potassium depletion and "symptomless hypotonicity' [3]) one factor has been a failure to re-expand a contracted extracellular fluid volume before giving 5% glucose solution The use of the term ' extracellular contraction in place of extracellular dehydration would help to emphasise the importance of repairing the osmotic framework of a contracted extracellular space

When I was a student the only intravenous fluid which we used was normal saline or glucose in normal saline While this may have prevented us treating or preventing intracellular underhydration it did at least, make unlikely the production of those very serious states of intracellular overhydration.

One other point needs to be emphasised with reference to extracellular contraction in the surgical patient This is that in most patients the loss of water is greater than that of sodium relative to the normal Na/water relationship of the E C F " [2] In other words, extracellular contraction in the surgical patient is usually hyper-osmotic or iso-osmotic and it follows that the serum Na level may be valueless in diagnosing the condition or in estimating the degree of sodium depletion which has to be made good. This point is clearly implicit in Professor Bull's lecture but it is a point that is sometimes overlooked the false assumption being made that because the serum Na level is normal or raised saline administration is not indicated.

This letter is little more than a quibble over terminology Terminology however may be important and I

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1 Black, D A K *Lancet* 1953 i 303 333

2 Le Quesne L P Fluid Balance in Surgical Practice London 1954

3 Wynn V., Rob C. G *Lancet* 1954 i 587

feel that there is a need today for one which is accurately defined, widely accepted, and reasonably descriptive, so that we can describe those water and electrolyte abnormalities which modern knowledge enables us to diagnose from the history and clinical and biochemical findings

Tyrone County Hospital, Omagh W S DAVIS

CANCER RESEARCH

SIR,—The time surely has come for a protest against the present methods of cancer research The large sums of money expended on the upkeep of the ever expanding wilderness which laboratory workers are creating would surely be better spent in building hospitals for patients suffering from malignant disease It is useless for anyone who has no knowledge of cancer as it is encountered clinically to endeavour to find the cause by experiments on animals

After long years of research, which have proved absolutely fruitless, it is high time that the laboratory method of investigation was abandoned In fact, quite a number of these laboratory workers have no medical qualifications, while several are not specially interested in cancer as a human disease Let us get back to the bedside and learn the earliest symptoms of cancer so that we may operate early and prolong the patient's life at least, if we cannot actually cure him

Edinburgh JAMES BURNET

SHOE DESIGN AND THE GREAT TOE

SIR,—In this correspondence particular emphasis has been laid on the effect of shoe shape on the hallux In my store we have perhaps an unusual opportunity for observing the effect of shoes on the development of children's feet, for we have a wide variety of British, Canadian, and American shoes Also we see infants before the weight-bearing stage and adolescents going through the transition from children's to adults' footwear

I suggest that no conclusive relation between the development of a foot and the shoes it wears can be obtained unless the condition of the foot at birth and before weight bearing is known More and more we are encouraging parents to let us see their infants' feet before they wear any kind of shoe so that we may be forewarned of possible difficulties that may be the result of intra-uterine distortion of the leg and foot and of noting the presence of any inherited characteristics

Apart from infants born with a degree of hallux valgus, there does seem to be some connection between even a mild degree of forefoot varus and subsequent realignment of the hallux when the forefoot varus persists We do not usually refer to this condition as a metatarsus varus, because it is really a complete "distortion" of the whole forefoot and mid tarsal section of the foot

There are two schools of thought regarding what, if anything, can and should be done about this type of foot, which we see in ever increasing numbers One practice is to put the foot into a shoe having a similarly "inswung" forepart, this seems to be a definite trend among British shoe designers The other view is that by stretching the foot in abduction and wearing shoes designed to provide the same amount of traction, the foot will revert to its normal alignment and consequently be less susceptible later to the influences of "out swung" shoes

Our experience of both methods is that the "inswung" shoe merely encourages the adducted position of the forefoot at a time when the foot is beginning to "set" When the child can no longer obtain such shoes, the change to conventional "outswung" is even more drastic, and distortion of the phalanges seem unavoidable Even if manipulation of the adducted forefoot is not carried out, the wearing of straight-lasted shoes, designed to direct the forefoot in a straight line, starting from the heel forward through the midtarsal section and finally at the head of the first metatarsal, gives some assurance that by the age of four the basic structure of the foot is as close as possible to what is generally accepted as "normal"

That shoes do influence foot shape appears The question seems to be "how much of the toes can be tolerated without causing function?" It is unrealistic to assume that the will ever accept the principle of "sensible" shoe worth-while period

I would like to mention the tremendous follow in Canada for the work of Mr Denis Browne. I more attention was given to minor congenit abnormalities attributed to intra uterine pressu these conditions were recognised from the sta measures taken to correct them, a large propo foot and shoe troubles would disappear

Kiddies' Shoeland,
North Vancouver,
British Columbia

ROY A

HALLUCINOGENIC DRUGS

SIR,—Professor Elkes and his colleagues have attention in their letter of April 2 to the dang treatment with lysergic acid diethylamide (LS Little has been published about the delayed re the report by Sandison et al [1] being a notable exc I should therefore like to record my interim find some of the phenomena Although they are b limited experience, they may serve as a warning, problems involved call urgently for investigation

The 8 patients in this series received LSD orally in *50–500 γ while fasting An interval of at least* sev separated doses after the trial ones Patients were all react with the minimum of interference necessary to injury or *accident Accounts of* experiences were o late on the day of administration in some cases, but found better to get written reports later and supplemen by oral discussion

Experience during the acute phase followed the pattern, but personal experience was dominant, even the early toxic hallucinatory patterns, som dream-like situations were acted out violently, lea from dreams before treatment began, and calling for pro measures

Experiences more than twenty-four hours afte administration of LSD could be grouped as follow

(1) *Mood swings* similar to those under acute drug occurred two or three days later It was not always to correlate these with environmental events. Both and euphoria occurred, the latter being often the less and insidious in its effects

(2) *Regression to childish behaviour* without other —e g, playing boats in the bath with the soap-dish quarter of an hour before realising that this was This was noted first nearly a week after taking any drug

(3) *Visual hallucinations* took several forms (*a*) *R to childhood* visual hallucinations, solid and coloured objects detached from their context—e g, a stepladder, elephant sitting on a tub These sometimes later built complete episodes, and were dated on the completion episode (*b*) *Complete episodes,* with auditory and hallucinations, usually growing from (*a*), and ac appropriate affect Development of experience had a sory quality, directing the attention, and excluding (*c*) *Hallucinations of fantasy,* comparable to dreams larly some "archetypes" (*d*) *Hallucinations of small* —crabs, cats, and insects (*e*) *Hallucinations of thou tents* in images—e g, a parade of various suicidal

It is doubtful whether (d) and (e) were due to LSD more like the familiar toxic type of hallucination, and after heavy sedation with barbiturates and insomnia patient insists that the hallucinations were similar to in acute LSD intoxication) They did not clear 'Parenterovite,' while the motor symptoms of barbi overdose did (*c*) occurred in a hysteric who had pre demonstrated a considerable capacity for visual pro In general it has been considered safer to accept as part LSD reaction, only experiences clearly related to p experiences, continuing previous dream material, or in the acute intoxication

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[1] Sandison R. A, Spencer, A M, Whitelaw J D A. J ment 1954, 100 491

Auditory hallucinations have been included above as a of complete episodes. Another form is the hearing of , often later related to emotions associated with earlier ences.

Body image and time changes —It was difficult to separate ling that the body was smaller from the idea that the as younger In some cases age seemed different without sation of bodily change; in others both were changed the patient felt smaller age two and could not talk to . But I have not yet seen a regression to childish speech haviour

Illusions and misinterpretations are mixed with hallu tion, and may lead into it Objects change in shape and ne meaningful images of past events or change into entations of associated ideas. Thus a pair of stork vases ed into babies." Other experiences were more within al range—e.g a plant against a shed appeared in the like a white unicorn

Somatic changes included subjective sensations of swell of the hands. Erythema of the fingers, previously noted e patient changed in character as relevant material ed. Objectively swelling and discoloration of one e followed an hallucinatory experience of violence by other (this was confirmed by the patient's husband)

Time and space —Quite early in treatment one patient ised that her judgment of speed was unreliable, and ould not cross roads when vehicles were in sight This ed for long periods At least during the more violent of abreaction time was indefinite. Preoccupation or mindedness may persist for weeks a patient may a bus to draw up and depart and then realise that she ssed it.

for the time relation of delayed reactions in rela to the ingestion of the drug they may continue the day, but in 1 case they were entirely inhibited for days.

od swings may occur at any point in treatment, even lower doses. Hallucinations and related experiences have noted only after repeated heavy doses. They have been also after 300 γ or higher doses, the lowest point at h continuous abreaction occurred was after a total of γ in three doses, following a break in treatment of weeks. Continuous abreaction has followed 1200 γ ree doses after a break of several weeks. The continu reaction may occur without preliminary and more brief ed reactions. In one case a further 1000 γ in three doses ed to establish a continuous reaction

1 case reactions continued for three weeks; treatment chlorpromazine was then started and it appeared to rol further reaction. It is important to bear in mind that patient's statement that reactions have ceased is not ble: they may begin again after an apparent return to al I could not at present put a limit to the time during h delayed reactions may appear

he factors which may affect delayed reactions ude:

1) *Interference* —Over-solicitous attention during the acute e upset 2 patients who could not let themselves go had reactions next day similar to those they would have , but they controlled these to some extent. In the light his experience it may be necessary to reconsider results ined by inquiry and tests during acute intoxication.

2) *Voluntary control.*—A patient apparently managed to n all reactions for five days after her last dose to prove she was fit to go home Others report that they can exert ited control after the acute intoxication is over in pany but must let go later *Hallucinations are often* whelming; they can be prevented to some extent by occupations but recur in intervals of relaxation and so fere with sleep

3) *Dosage.*—2 patients who had continuous reactions had onged treatment with doses of 200–400 γ over several s. The total doses were 4200 γ and 1000 γ respectively both had a break of three or more weeks during treatment

n the management of delayed reactions heavy seda n with barbiturates proved useless for stopping the ces though it appeared to 'cushion' some of the periences. This was possibly due to these patients ing previously had prolonged barbiturate narcosis d also barbiturates as sedatives at other times

Paraldehyde (5 ml intramuscularly) gave some sleep but it was inadequate alone or with bromide Methylpentynol ("Oblivon") gave rather better results with bromide Potassium bromide (gr 20 t.d.s) appeared useful as a basic sedative The best results were obtained with chlorpromazine (50 mg intramuscularly) (a personal communication from Dr Sandison suggested this, since chlorpromazine reverses electro-encephalogram changes due to LSD) We have not yet been able to demonstrate this effect in the E.E.G., but we are not yet sure that E.E.G. changes persist in the delayed continuous reaction

It may be useful to summarise the possible dangers

(1) In mood swings the dangers of depression are obvious; and euphoria may be also embarrassing

(2) Time and space distortion are an obvious danger in traffic.

(3) Hallucinations are perilous out of doors and socially embarrassing

(4) Insomnia is a great difficulty; reactions are particularly likely to occur when relaxing for sleep

(5) Impulsive behaviour, wandering and absentmindedness may all create difficulty

Rainhill Hospital,
near Liverpool

H ASTLEY COOPER.

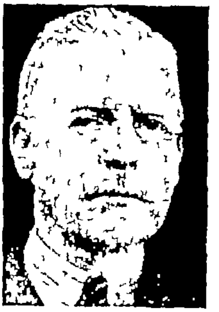
Obituary

HARRY JAMES RAE

M.C. M.A M.B Aberd D.P.H

Dr Rae who was formerly medical officer of health of the city and counties of Aberdeen and Kincardine died in his home in Aberdeen on May 7 at the age of 69

He was born in Woodside Aberdeen and he graduated M.A. from the University of Aberdeen in 1907, and M.B with honours four years later After graduation he was appointed resident to Mr John Scott Riddell at the Aberdeen Royal Infirmary and the help and guidance he gave to the students on his ward is still remembered He took the D.P.H in 1914 but before he was fairly launched on a public health career he joined the R.A.M.C For his work with a field ambulance in Palestine he was awarded the military cross and was mentioned in despatches



After he was demobilised he resumed his work as tuberculosis officer in Aberdeenshire later succeeding Dr Watt as county M.O.H In 1929 he was appointed medical officer of health of the City of Aberdeen in succession to John Parlane Kinloch who had been appointed chief medical officer to the Department of Health for Scotland In 1930 Rae became medical officer also of the county of Kincardine He was also part-time lecturer in public health at the University of Aberdeen a post which medical officers of health of the city have always held

Thanks to his organising ability and foresight all the first aid posts were ready in these north-east towns before the outbreak of war in 1939 and his organisation never broke down during the eighteen months of heavy raiding in 1939–41

When the Royal Family were spending their annual holiday on Deeside in 1941 he supervised the immunisation against diphtheria of Princess Elizabeth and Princess Margaret He was made an honorary physician to King George VI and later to the Queen

After his retirement in 1952 he found time and interest for fresh responsibilities. For the past two years he had been visitor and inspector in public health and social medicine to the universities and medical schools for the General Medical Council. He was also a past president of the Royal Sanitary Association of Scotland and a member of the town council of Aberdeen

A U W writes The medical practitioners in the north east of Scotland—especially those of the older groups—were saddened by the death of Dr H J Rae

His end marks the passing of a great era—the days of the medical officers of health who were administrators, clinicians, and advisory consultants in all matters relating to public health Though always fully and busily engaged in high undertakings, he 'never despised the day of small things', and his kindness and ready help, always so quickly and so courteously given to the country general practitioners, were significant of the true nobility of his character"

Dr Rae is survived by his wife, two sons, and two daughters One of his sons is Dr W J W Rae of Aberdeen, and a daughter is Dr Isobel Margetts of Nottingham

JOHN LOWE

C B E, M C, M D Birm, F R C P

Dr Lowe was medical secretary of the British Empire Leprosy Relief Association for just over a year, but he brought to his appointment many years of clinical experience in India and Africa His death on May 13, at the age of 57, is a loss to the campaign against leprosy

He was born in 1898, and he went straight from King Edward's School, Birmingham, into the Army to serve in France throughout the first world war He rose to the rank of captain in the King's Own Lancaster Regiment and won the M C He returned to study medicine at Birmingham University and graduated M B in 1922 The next year he went to India as a Methodist medical missionary to the leprosarium at Ditchpali in the Nizam's dominions There he also studied malaria, on which he later wrote the thesis which gained him the M D in 1937

In 1932 Lowe joined the research staff of the Calcutta School of Tropical Medicine, and three years later when Muir retired he succeeded him as head of the leprosy department In 1943 he was appointed to the chair of tropical medicine at the school, but in this post he still maintained his interest in the leprosy department

The previous year he had been appointed assistant editor of the *Indian Medical Gazette*, and in 1943 he succeeded Dr Everard Napier as editor The introduction of the sulphone drugs led him to return to clinical work, this time in Africa On leaving India in 1947 he was awarded the Kaiser-i-Hind gold medal, and the same year he took the M R C P For the next six years he was in charge of the research unit of the leprosy settlement at Uzuakoli in Nigeria The pioneer work which he did there on the essential action of the basic substance, dapsone, was of the greatest practical importance When he retired in 1954 he was appointed C B.E and elected F R C P On his return to this country he took over the medical secretaryship of B E L R A. and the editorship of the *Leprosy Review*

L E N recalls that his first association with Lowe was through a paper submitted for publication "This paper, which was on pellagra among leprosy patients in an institution in the Deccan where he was at that time working, showed him to be an astute observer and a clear thinker, this first impression was confirmed constantly throughout my association with him As an editorial colleague, he was most refreshing, his fearless criticism gave one great confidence, for one knew that one would not be allowed to get away with little unorthodoxies if he considered them beyond the pale of respectable medical writing He himself was a facile and clear writer

"Perhaps his most outstanding characteristic was that he was a great debunker, but he was always careful how he did his debunking Though a good Christian and closely associated with the missionary movement in India for many years, he never allowed his zeal to cloud his judgment In his early days he confided in me that he did not believe that the antileprotics then in use had the slightest direct effect on the course of the disease, but, though he desisted from joining the chorus of praise at that time showered on these ineffective drugs, he withheld his active criticism, he knew that faith in these drugs was the corner-stone of leprosy work throughout the world, and that to shake it publicly would do untold harm, not only to hundreds of thousands of leprous patients, but to the whole movement When he took over from me as professor of tropical medicine, he was, I know, thankful to get some respite from this work and the conflict that it must have engendered within him. Later, with the advent and development of the sul he saw new hope and readily returned to wh work on leprosy with—one should add—cons effect, it gave him further opportunity for deb into which this time he could put his whole heart."

P M-B writes "Lowe was a stocky, solid, r man holding strong convictions His rather personality was an outward mask and concealed a of great worth and determination His outstandin age was shown when once he was stricken dow paralysis during one of his periods of leave from and had for some time to live in an iron lung Fu his determination carried him through and he complete recovery He was one of those good C who devoted their lives to the study of leprosy, making any great outward show about it—and, he will long be remembered for the good original that he had done to alleviate this disease. It wa who made the assessment of the long term with D D S possible, it was he, with Dharme standardised the antigen for the Mitsuda reacti put it on a rational basis for diagnosis it was enthusiastically took up the question of B C G into the study of leprosy and indicated its prophylactic action Indeed all Lowe's writin there were many, were of a high order and much solid material"

Dr Lowe leaves a widow and two sons, both of are doctors

CLAUD FRANCIS FOTHERGILL

M A., M B Camb

Dr Fothergill, who died on May 6, at his Chorley Wood, was well known as doctor, chur and Alpine climber

He was born in 1878 at Tunbridge Wells and he st medicine at Emmanuel College, Cambridge, and Hospital After qualifying in 1906 he was acc a candidate by the Church Missionary Society, accident, while operating, led to septicæmia and ill kept him in this country In 1907 he settled in in Chorley Wood His interest in neurology and p logy was fostered by his experience in the 1914-18 and he became a consultant for shell-shock cases Ministry of Pensions For a year he was also in of the neurological department at Guy's and he was in charge of a psychological clinic of the M of Pensions and neurologist to the Ministry's appeal board He also had a private consulting

Outside his medical interests he gave much time energy to the Camps and Tours Union, and he hi led nine parties to the Holy Land He also extensive tours in this country to lecture to schoo churches on these visits He was an enthusiastic taineer, a member of the Alpine Club, and a vice-p of the Association of British Members of the Alpine Club, and he led many of the moun tours of the union, especially to Switzerland

C M-D, who will always be *grateful* to Foth for introducing him to Switzerland, writes "Foth was a *first-rate climber, so much so* that I doubt wh there is any major peak in the Alps that he has ascended When climbing he always wore a stiff even on the most severe ascents maintaining that kept him cooler and gave ventilation to his neck matter how exhausted any climber might be, Foth always forbade alcohol as a stimulant, for he found sugar was more effective and more prolonged in action My outstanding memory of him was the his practical Christian and evangelical faith. never was a more fervent or zealous preacher of gospel His message was always from the Bible like Billy Graham in this generation, whenever he at a meeting the substance of his address was Bible says' The private parties that he took to Sw land always ended each day with prayers and an ad more often than not by Fothergill himself

"The last time I met him was immediately after war, when we had been denied our annual visits Switzerland for so many years We each took a party out the moment Continental travel was perm and we shared the booking of a special train. On t on he was just the same Fothergill as I knew y five years before—a trifle older perhaps but wise exactly the same—even to the stiff collar'

1908 Dr Fothergill married Enid Annesley daughter late General John Gell She survives him with sons and a daughter

ETHEL CASSIE
O.B.E. M.D Edin. D.P.H

HOUGH an outstanding administrator Dr Ethel e did not have a bureaucratic mind, and her achieves in the Birmingham maternity and child welfare rtment were the result of an imaginative vision ined with a deep and genuine sympathy for the lems of the working-class mothers and an under ding of their needs

e was born in 1882 and graduated M.B in the ersity of Edinburgh in 1906 Her interest in social preventive medicine was early aroused and the wing year she took the D.P.H Later she became al officer of health for the county burghs of Clack annshire In 1921 she was appointed assistant ical officer of health for maternity and child welfare Birmingham.

ith the sympathy and support of her chief, Sir John rtson, she began her pioneer work. During the next ty years 25 welfare centres were opened 13 of them pecially constructed model buildings A babies ital with some 90 beds and a convalescent home for hers and babies were also opened Her book on *ernity and Child Welfare* was published in 1920 ing a visit to the United States she made a study of ature babies which led in 1930 to the opening in ingham of a ward for premature babies—now known the Sorrento unit. In 1935 she introduced the ingham foster mother scheme the first of its kind his country In the early years of the late war she ed 80 day nurseries and 6 residential nurseries for children of war-workers. For her services to maternity child welfare she was appointed O.B.E.

colleague writes 'At the time of Dr Cassie's ointment to Birmingham the health visitors were teer workers who shared her enthusiasm and wholetedly devoted themselves to carrying out her idea t the welfare centres should be places where mother child would not only receive advice and health ation but feel happy and at home. There was much the artist in her nature and she insisted that the tres should not only be useful, but beautiful, a fact ch the mothers appreciated It was a source of regret her that with the growth of her department, her ministrative work increased so much that she was iged to give up her clinical work and lose the personal tact with mothers and children which she so greatly ned But she never lost her interest in clinical medi e; it was perhaps her ability to see disease as a duct of environment which turned what might have n an outstanding physician towards preventive dicine She leaves behind a memorable record of vice to women and children'

r Cassie retired in 1948 owing to ill health, and she d on May 6 at her country home in Oxfordshire

Appointments

ITLE I R, M.A Camb, M.R.C.S., D.M.R.E consultant radiologist, Plymouth clinical area

st Anglian Regional Hospital Board:

LAN JOHN M.B Aberd, D.M.R.D registrar in radiology Norfolk and Norwich Hospital

TCHLOW J M, M.B. Leeds: registrar in psychiatry Hellesdon Hospital Norwich

PARTH H E N L.M.S.S.A D.M.R.T registrar Norfolk and Norwich Hospital, and Jenny Lind Hospital Norwich

spital for Sick Children Great Ormond Street, London

THROW, D G M C B.M Oxfd M.R.C.P house physician

DONSON MARY B M.B Camb: resident M.O Tadworth Court.

FRIEDLANDER, Louis M.B Witw'srand M.R.C.S D.C.H: asst. medical registrar

FIRTH KATHLEEN A M., M.B Lond F.R.C.S: senior surgical registrar

HARRATT ANN M.B Lond D.O: part time senior registrar ophthalmic department

WILKS JOHN M.B. Lond. F.R.C.S. senior surgical registrar

Notes and News

SOCIAL CLUBS FOR EPILEPTICS

MANY epileptics, capable of leading normal lives are shy of mixing with people because they have for so long met with public prejudice To help them the British Epilepsy Association is starting a chain of social clubs Four clubs have already been opened in London and there are also clubs in Birmingham, Salford and Sheffield

The South London Social Club (54 Ormiston Road West combe Park, S.E 10) is open every Monday from 6 30 P.M until 10 P.M to men and women of all ages. Indoor games vary from cards to billiards refreshments are served free save for a voluntary collection and there is no entrance fee or subscription. The other clubs in London are the North London Social Club L.C.C Welfare Centre Corsica Street Highbury N the Chelsea Club King's Mead Sydney Street Chelsea; the Bethnal Green Social Club Eastbourne House Youth Centre Bullards Place E.2

The clubs are growing steadily but they need the support of epileptics and their friends. Further particulars may be had from the association 136 George Street, London, W 1

PRE-WAR DIETS

A REPORT lately published[1] records the details of the diets of 1352 families in the United Kingdom in the years 1937–39 Only those families with children were selected for study; but they were representative of the economic conditions of the time and the results are analysed for six different economic groups classified on average expenditure on food per head per week. The survey was planned by Lord Boyd Orr and it confirms and strengthens the conclusions set out in his book *Food Health and Income*, published in 1936 A preliminary report of the findings was available early in the war

In a preface, Lord Woolton our war time Minister of Food pays tribute to the work of Boyd Orr and his colleagues in providing essential information on which the food policy of the country was based The report, he says is "a unique record unique because it profoundly affected the life of a nation during a world conflagration. Fifteen years on, the report is necessarily mainly of historical interest In 45 well-set-out tables there are records of the foods consumed analyses of the diets in terms of nutrients and heights weights, cristal heights and hæmoglobin levels of the children. There are also details of the incidence of certain clinical conditions amongst the children such as chronic upper respiratory catarrh, knock knee skeletal deformities, otitis media, pyogenic infections and bronchitis.

University of Birmingham

Dr A. G W Whitfield has been appointed chairman of the board of graduate studies from Oct 1

University of Dublin

On May 12 the following degrees were conferred:

M.D—Margaret K B Knox F du P Meiring

M B B Ch B A O—P R D Black Jean R. Ellis A C A Hempel

Royal College of Physicians of London

On Tuesday June 21 at 5 P.M at the college, Pall Mall East, S W 1 Dr K M A Perry will give the Ernestine Henry lecture on Pulmonary Disease associated with Metallic Oxides.

Royal College of Surgeons of Edinburgh

At a meeting of the college held on May 11 with Prof Walter Mercer the president in the chair the following were admitted to the fellowship:

L I Burt Priya Brata Chakravarti D L Cornish Michael Dinner W G de Haas Sin Yang Fang I C Grayson A A Gunn T B Hogarth Michael Katzen Myron Lange J A MacDougall T J McNair Maung Kyaw Maung I G Nairn R L Plowman A F Richardson E H Rosenberg F J Sanders S R Shar Jack Stevens T J Thwaite J B Walker

Society for Endocrinology

On Tuesday May 24 at 5 P.M., at 1 Wimpole Street, London W 1 Dr A Lacassagne (Paris) will give a lecture on Endocrine Factors concerned in the Genesis of Experimental Mammary Carcinoma.

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[1] Family Diet and Health in Pre-war Britain A Dietary and Clinical Survey Report to the Carnegie United Kingdom Trust from the Rowett Research Institute 1955 Pp 164 Obtainable free from the Carnegie United Kingdom Trust Comely Park House Dunfermline Fife

Royal College of Surgeons of England

At a meeting of the college on May 12, with Sir Harry Platt, the president, in the chair, the following were admitted as elected fellows Dr R D Langdale Kelham (Roehampton), Dr L S Debenham (Scarborough), Prof J McCunn (Royal Veterinary College) and Dr Gwen Hilton (University College Hospital)

Dr L C Thomson was appointed as the first Edridge Green lecturer, and Prof Geoffrey Hadfield and Dr Leslie Foulds were appointed as *Imperial Cancer Research Fund* lecturers Dr J M French was awarded a Mackenzie Mackinnon research fellowship The Begley prize was awarded to Malcolm Swann

Licences to practise were conferred on the candidates named in the report of a comitia of the Royal College of Physicians (*Lancet*, May 7, 1955, p 978) and on N A Waring, who have passed the final examination of the conjoint board A diploma in child health was awarded to the candidate named in the same report

Diplomas of fellowship in the faculty of anæsthetists were granted to the following

P J Horsey M D Mehta, France Brun, A V Jenkins William Brooks Betty R Warltier, W R Lamb P D Kempthorne B L Day G G Harrison A G MacKinnon H P Penn, D B Scott L M V Attygalle, G W Black Peter Hall A M Reid, Peter Stuart, I D Campbell, Brenda M Dempsey, Margaret M Fitzgerald, P J Roffey Rosemary A Fraser

Tribute to Professor Vining

On May 6, in the children's ward of the Dewsbury General Hospital, members of the consultant and nursing staff and local general practitioners entertained Prof C W Vining when a plaque was unveiled to commemorate his work as pædiatrician to hospitals in the district from 1930 to 1953

London Amateur Boxing Association

A meeting of the medical officers of this association is to be held at 69, Victoria Street, London, S W 1, on Tuesday, May 24, at 8 P M, when Mr A Rugg Gunn will speak on eye injuries The meeting is open to all doctors.

World Health Assembly

The eighth World Health Assembly opened in Mexico City on May 10 Dr Ignacio Morones Prieto, minister of health and welfare of the government of Mexico, was elected president, and Dr S Al Wahbi (Iraq), Dr J Gratzer (Austria), and Sir Arcot Mudaliar (India) were elected vice presidents

Grants for Research on Leukæmia

The Robert Roesler de Villiers Foundation of New York will shortly make grants in aid (maximum about £350) in support of research on leukæmia Investigators in the United Kingdom should apply to the regius professor of physic, University Department of Medicine, Tennis Court Road, Cambridge, before June 15

Secondary School for Spastics

The National Spastics Society has opened a secondary school for spastics at Dene Park, Tonbridge, Kent The school, which will be known as the Thomas Delarue School, will take 18 children this term, and it is hoped eventually to accommodate 45 handicapped boys and girls Education up to general certificate level, combined with treatment, will be provided A second school will be opened on May 11 in Cardiff The society hopes to open three more schools this year Further information may be had from Mr C Pritchard, National Spastics Society, 28, Fitzroy Square, London, W 1

Harveian Society of London

The society's Buckston Browne Gray Hill dinner at the Royal College of Surgeons on May 13 was a medicolegal occasion Sir Fred Pritchard, Q C, proposing The Society, hoped for closer ties between the two professions, and he looked forward to the time when this friendly coöperation would make a substantial contribution to improving the lot of the people for whom *laws were made* He referred especially to the rules about the law of insanity which had held good (or bad, many would say) for so long, and which would continue to do so unless the two professions got together to change them. In his reply, Mr A Dickson Wright, the society's president reinforced Sir Fred's call for a more effective liaison between Medicine and the Law, and later Mr H Edmund Davies, Q C, added his counsel in support of the case Mr Davies was replying to a warm welcome extended to The Guests by Dr D Geraint James

Mental Hospital as a Therapeutic Community

A weekend course on this subject for psychiatrists, hospital nurses, education officers, social workers, oc therapists, and mental hospital staff will be held at P Manor Residential College, Burton, Wirral, Cheshire, June 3 to 5 Further particulars may be had from Dr Frost, Deva Hospital, Liverpool Road, Chester

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Dr Hilda Roberts has received a research grant of the the National Birthday Trust Fund

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Diary of the Week

MAY 22 TO 28

Monday, 23rd

POSTGRADUATE MEDICAL SCHOOL OF LONDON, Ducane Ro
4 P M Dr A C Corcoran (Cleveland) Current Develo
Hypertension
UNIVERSITY OF LONDON
5 30 P.M (London School of Hygiene and Tropical Me
Keppel Street W C 1) Dr R. J Huebner (Be
Newly Recognised Respiratory Viruses and the Se
Diseases which they Cause
BRITISH ASSOCIATION OF SPORT AND MEDICINE
8 P M (Middlesex Hospital Medical School Mortimer
W 1) Mr Philip Wiles Athletic Injuries as Seen
Hospital
MANCHESTER MEDICAL SOCIETY, Medical School, Manchester
4 30 P.M *General Practice* Dr W E Savage, Dr Simon Fr
Insomnia

Tuesday, 24th

ROYAL COLLEGE OF SURGEONS OF ENGLAND Lincoln's Inn
W C 2
5 P M Mr H G Hanley Surgery of Male Sub
(Hunterian lecture)
UNIVERSITY COLLEGE, Gower Street W C 1
5 15 P M Prof R A McCance F R S Metabolism and
Function in the First Few Days of Life (Cushny lec
ST MARY'S HOSPITAL MEDICAL SCHOOL, Paddington, W 2
5 P.M Dr Corcoran Evaluation of Antihypertensive Dr
WRIGHT FLEMING INSTITUTE OF MICROBIOLOGY, St. Mary's Ho
Medical School
5 P.M. Lord Stamp Action of Bacterial Enzymes on Imm
Antigens
INSTITUTE OF DERMATOLOGY, St John's Hospital Lisle S
W C 2
5 30 P M Dr W N Goldsmith Skin Lesions in Me
Disorders
SOCIETY FOR ENDOCRINOLOGY
5 P M (1 Wimpole Street, W 1) Dr A Lacassagne (P
Endocrine Factors concerned in the Genesis of E
mental Mammary Carcinoma

Wednesday, 25th

POSTGRADUATE MEDICAL SCHOOL OF LONDON
2 P.M. Dr J Anderson Erythroblastosis and its Imp
Pathological Processes
ROYAL SOCIETY OF MEDICINE 1, Wimpole Street W 1
5 P M *Comparative Medicine* Dr E L Taylor, Prof A A
Mr F C Bawden Host parasitic Relationships
5 P.M *Endocrinology* Dr W O Nelson Testicular Phy
8 P.M *Pædiatrics* Dr E G L Bywaters, Dr B
Schlesinger Dr Gerald Thomas Juvenile Rheumat
ST MARY'S HOSPITAL MEDICAL SCHOOL
5 P M Prof. T N A Jeffcoate Pruritus Vulvæ.
INSTITUTE OF DERMATOLOGY
5 30 P M Dr Henry Haber Localised Diseases of the Co
EUGENICS SOCIETY
5 30 P M (Burlington House, W 1) Mr J A. H Wate
PH D Twins and Genetics
MANCHESTER MEDICAL SOCIETY
4 30 P M *Pathology* Dr G B Manning Forensic Medi
BIRMINGHAM MEDICAL INSTITUTE 154, Great Charles
Birmingham 3
8 P.M *Psychiatry* Dr J D Sutherland Psychother
Provisions in a National Health Service

Thursday, 26th

ROYAL COLLEGE OF SURGEONS OF ENGLAND
3 45 P.M Dr H Stansfield Visual Pathway (Arnott d
tration)
POSTGRADUATE MEDICAL SCHOOL OF LONDON
4 P M. Dr Edwin Clarke Epilepsy
INSTITUTE OF DERMATOLOGY
5 30 P.M Dr J O Oliver Blood Coagulation.
NUFFIELD ORTHOPÆDIC CENTRE, Wingfield Morris Ort
Hospital Oxford
8 30 P.M Prof J Trueta *Reflections on Bone Grow*
Eight Years Study
UNIVERSITY OF ST ANDREWS Medical School Small's
Dundee
5 P.M Mr A. Dickson Wright Sciatica of the Arm.

Friday, 27th

POSTGRADUATE MEDICAL SCHOOL OF LONDON
2 P M Mr J G Yates Bell Treatment of Hydronephro
UNIVERSITY COLLEGE
5 15 P M Prof M. L Rosenheim Functional Aspects of
Failure (Cushny lecture)

HLORPROMAZINE IN PSYCHIATRY

G F VAUGHAN
M.B Lond., M.R C P D.P.M
REGISTRAR IN PSYCHIATRY GUY S HOSPITAL, LONDON AND BEXLEY HOSPITAL, KENT

D M LEIBERMAN
M.D B Sc. Leeds, M.R.C.P D.P.M
ONSULTANT PSYCHIATRIST BEXLEY HOSPITAL AND ST ALFEGE S HOSPITAL, GREENWICH

L C COOK
M.D Camb D.P.M.
IAN SUPERINTENDENT BEXLEY HOSPITAL ASSOCIATE ICIAN DEPARTMENT OF PSYCHOLOGICAL MEDICINE, GUY S HOSPITAL

ORPROMAZINE (Largactil Thorazine, Mega) has been used in psychiatry since 1952 and it becoming possible to assess its position in relation er psychiatric treatments

Chemical and Pharmacological Properties

some time it has been known that the anti aine drugs have multiple pharmacological properties s their main action; for example some have ine-like properties some atropine like while yet have the actions of quinidine or pethidine All substances show in various degrees anti-adrenaline, cetylcholine, and anti histamine activity (Burn utta 1948) In addition, some of the anti histamine , such as diphenhydramine (Benadryl) and ethazine ('Phenergan') have a sedative action cing drowsiness and sleep after an initial period of ria. Chemically chlorpromazine is closely related e anti histamine drug promethazine and to the arkinsonism drug ethopropazine hydrochloride ivane')

chemical and pharmacological properties have been bed in detail by Courvoisier *et al* (1953) and eo (1954)

appears to be rapidly absorbed from the intestine the oral and intravenous doses required to produce toms of toxicity *are about equal* with *similar time* als from administration to the onset of symptoms action is maximal at one hour with appreciable s at six hours *and some activity* at twenty four . Since only 7% of the doses administered is ted in the urine in three days most of the drug is mably metabolised in the body though the route known

lorpromazine has a sedative action and under its nce the patient appears dreamy calm listless or otic and may *complain of cold* muscular weakness thirst (Dundee 1954) The blood pressure is labile ally induced vomiting is inhibited and the central n of alcohol barbiturates anæsthetic agents, and esics is potentiated (Beard 1954) The sleep activity n by electro-encephalography when these drugs used is like that of physiological sleep and quite e that seen with *barbiturate induced sleep* (Terzian)

ntal conditions reported to have been treated sfully with chlorpromazine include mania, hypo a, and psychomotor excitement (Lehmann and ahan 1954) confusional states (Delay et al. 1952a b Martin 1954) acute and chronic alcoholism rt et al 1954 Cummins and Friend 1954) *agitated* ssion, melancholia chronic hallucinatory psychosis etable in omnia and intractable pain and neuralgia ald and Bouttier 1953) and various neuroses kelman 1951 Sigwald and Bouttier 1953 Azima Ogle 1954 Garmany et al 1954)

6874

The clinical effect, which apparently enables the drug to benefit so many different conditions seems to consist in a reduction of tension, a loss of preoccupation and a reduction in psychomotor activity (Elkes and Elkes 1954) Manic states have been said to be particularly susceptible to the action of chlorpromazine (Lehmann and Hanrahan 1954 Martin 1954 Cossa et al 1953) Elkes and Elkes (1954) in a small controlled series found it of particular benefit in reducing the overactivity and *agitation of chronic psychotic patients* Several workers have applied this with benefit to similarly excited and overactive schizophrenics (Staehelin and Kielholtz 1953 Arnold et al 1953) This beneficial effect is especially evident in chronic cases considered incurable but only where the underlying personality has not been damaged (Sal y Rosas et al. 1954) Chlorpromazine influences particular groups of symptoms and cuts across diagnostic categories, an effect seen in other forms of physical therapy used in psychiatry—e g., prefrontal leucotomy

We *report here the effect of the drug on 224 female* patients in Bexley Mental Hospital. They formed a consecutive series and include 24 cases with controls A small group of 23 male patients was similarly observed and the results (not presented) differed in no way from those obtained in the females.

Material and Methods

Group A comprised 200 patients placed consecutively on treatment with chlorpromazine This group contained psychotic and some neurotic *patients and* was *typical* of the patients under treatment in the hospital Treatment was initiated by the doctor concerned with each case, but subsequent assessment was made by the *investigators in the following* manner Patients who showed a favourable response were placed on placebo tablets identical in appearance with the chlorpromazine *tablets, for a month* and the effect was noted Then either the active tablets were administered again or if improvement was still *maintained* the treatment was discontinued

Group B comprised 48 patients selected for treatment largely because they were restless agitated and showed psychomotor excitement In this respect they *formed* a sample of the most chronic and *intractable* the hospital patients and were unpromising from the therapeutic point of view By random selection 24 of these were started on chlorpromazine and 24 *on* the placebo the hospital pharmacist alone knowing which patients were receiving chlorpromazine and which the placebo

Methods of Administration

Chlorpromazine was given either by intramuscular injection followed by oral administration of tablets or by the oral route alone With the former method up to 150 mg daily usually in three *doses, was injected for* four days. No special precautions about rest in bed were taken, but the nurses were made aware *of the* possibility of faintness after *injections* and told to rest the patients if this appeared necessary Owing to the low pH the solution is irritant to the tissues (*Cloutier* 1953) but in practice if the chlorpromazine is given by deep intramuscular injection few patients complain of soreness, though indurated areas are produced in some and may persist In 1 case out of 33 thus treated a cold abscess formed

Many workers have commented on the more potent effect of parenteral administration—e g *Martin (1954)* and Charatan (1954) In the present series of 33 patients started on injections and then treated by oral *administra*tion 13 were either symptom free or much improved *The corresponding figure for purely oral* administration is 43 symptom free or *much improved* out of 167 treated This is no more than suggestive that the parenteral route may be the more potent

In some patients the curious phenomenon was observed that, though they did not respond to initial oral administration, an effect produced by parenteral administration could be maintained by an oral dose

The dosage by mouth was started at 75 or 150 mg daily in three doses, and varied, according to the response, up to 450 mg daily. Most of the patients received 150–200 mg of the drug daily

Results

GROUP A

This group consisted of 200 female inpatients selected only because they were consecutively placed on treatment with chlorpromazine This was instituted by a number of different doctors for a variety of conditions

Table I shows that of the 200 cases 124 (62%) improved, 56 (28%) becoming much improved or symptom-free, and 76 (38%) remained unimproved This assessment was made on the most stringent grounds and is of more value when it is appreciated that the majority of these patients were chronic hospital patients (Affective states mean age 53, mean duration of stay in hospital 3 8 years Miscellaneous states mean age 45, mean duration of stay 1 6 years Schizophrenic states mean age 42, mean duration of stay 10 3 years)

TABLE I—RESULTS OF CHLORPROMAZINE IN 200 CONSECUTIVE CASES

Diagnosis	Changes in symptoms				Total
	No change	Improved	Much improved	Symptom free	
Schizophrenic states	31	44	26	2	103
Affective states	36	19	18	7	80
Miscellaneous states	9	5	3	0	17
	76	68	47	9	200

Schizophrenic Group

Although examples of all types of schizophrenia were included, the great majority of the patients in this group were catatonic or paranoid schizophrenics showing some of the symptoms of excitement, aggressiveness, overactivity, noisiness, and hallucinations 72 (70%) showed some improvement, and 26 of these were greatly improved, 2 being rendered symptom-free Apart from certain cases of mania (mentioned below) the most dramatic responses to chlorpromazine were in this group

To obtain a clearer picture of the nature of the response 25 of this group were selected for closer examination These patients had shown the greatest degree of improvement and were rated as regards their main before and after treatment (table II)

TABLE III—EFFECT OF CHLORPROMAZINE IN 80 CASES AFFECTIVE DISORDER

Diagnosis	Changes in symptoms			
	No change	Improved	Much improved	Symptom free
Simple depression	5	7	6	3
Agitated depression	2	4	2	3
Depression with hypochondriasis	7	1	0	0
Neurotic depression	13	5	3	1
Depression with major organic disease	2	1	1	0
Mania	7	1	6	0

The symptoms most often improved were ness 17/17, noisiness 15/15, overactivity 13/13, ag 6/6, tension 5/5, depression 4/4, incontinence, incapability of occupation 15/16, disturbed sleep and disturbed appetite 9/10 The mean age was 43 the average duration of stay in hospital 12 8 Generally speaking chlorpromazine controlled p motor excitement and agitation, aggressiveness, tension, and allowed better rapport, enabling the to become occupied and resocialised On the hand, the basic schizophrenic symptoms—thought turbance, delusions, and hallucinations—appeared much less influenced, and continued, though fre reduced in intensity, even though the general and other individual symptoms had much im Other authors have commented on the use of promazine for insomnia, either alone or as a of other sedatives, and in our group of disturbed ch patients less night sedation was necessary while were on chlorpromazine therapy

In this group all the patients relapsed sooner or usually in from one to three weeks after the su of a placebo, and none maintained their improvement more than three months after chlorpromazine had withheld

The most important feature in the action of promazine on the chronic schizophrenic is the ment in his ability to enter into activities p impossible This is of immense benefit and can rap lead to a complete change in the character of a chr ward It is comparable to the remarkable effects duced in suitable cases by maintenance electroconv therapy (E C T) (Moore 1943, Shoor and Adams 195

Some chronic schizophrenic patients had been rece chlorpromazine for more than a year but relapsed w a few weeks of discontinuing treatment How great their improvement, with 2 possible excep

TABLE II—ANALYSIS OF SYMPTOMS IN SCHIZOPHRENICS RESPONDING TO CHLORPROMAZINE

Symptom	Case no																									In of improv
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	
Depressed				X																		X	X̲		X	[illegible]
Retarded				X̲																	S					[illegible]
Overactive			X		X	X			X	X	X				X	X		X	X	X		X	X			[illegible]
Underactive		X		X		O						X	X				X				S			X	X̲	[illegible]
Agitated	X̲								X					X̲					X				X		X̲	[illegible]
Perplexed	S													X̲			S								X̲	[illegible]
Aggressive	X̲	X̲	X̲		X̲	X̲		X		X̲	X̲	X̲	X		X	X̲				X̲	X	X		X̲	X̲	[illegible]
Noisy	X̲	X̲	X̲	X̲	X̲	X̲	X̲			X̲	X̲	X̲				X̲		X	X	X̲				X̲		[illegible]
Hallucinated	S	S	S	S	X̲		S	S					X		X̲	X̲				S		X		X̲		[illegible]
Grossly deluded		X̲		S			S	S	S			S			X̲	S	S		X̲	S				X̲		[illegible]
Gross thought disorder	S		X		X		S	S	S	S		S	X	S	X̲	S	S	S	X̲	X̲	S	S	X	X̲		[illegible]
Tense									X̲		X									X̲		X̲			X̲	[illegible]
Withdrawn	X̲	S				O		X̲				X̲	X	X		S				S	S	X̲		X̲		[illegible]
Disturbed sleep	X̲	X̲	S		X			X̲		X̲		X̲			X	X̲		S						X̲	X̲	[illegible]
Disturbed appetite	X̲		X							X̲		X̲	X	S		X̲	X							X̲	X̲	[illegible]
Incontinent					X̲									X̲	X̲											[illegible]
Unoccupied	S	X̲	X̲		X̲	O		X̲		X̲	X	X			X̲	X̲	X̲	X	X	X̲				X̲	X̲	[illegible]
Socially unacceptable	X̲	X̲	X̲	S	X̲	S	S	S	S	S		S	X	X	X̲	S	S			X̲				X̲	X̲	[illegible]

X̲ symptom much improved O new and unwanted symptom S, symptom present but unchanged ioned below, careful examination always revealed the patient still had disordered thought processes ugh able to ignore them No basic qualitative go took place in the underlying schizophrenic ess.

e 2 schizophrenic patients classed as clinically tom free are of particular interest in this connection following case typifies both.

woman aged 32, was admitted to hospital in 1949 led manneristic, and hallucinated; but there was a uating affective element in her illness, and when at her she was able to leave the hospital to visit relations for ends. During the last four years she had become increas deluded, hallucinated, and aggressive; much of her h was crudely sexual and there were phases of catatonic ement. She improved temporarily with courses of E C T, over the years there was a steady deterioration in her viour On chlorpromazine 200 mg daily by mouth for months she made an apparently complete recovery admitted to having been deluded saying that her thoughts eemed outside her control. Yet she gave the impression all was not quite well. Occasionally there was a suggestion her thoughts were oblique and her mood inappropriate remained well for ten weeks without chlorpromazine ng the hospital whenever she wished for shopping and to her home She was then sent home on trial but sed acutely within a few weeks. On further chlorpro ine by mouth she showed no improvement, but she onded to intramuscular chlorpromazine given for three

dive Group

his group consisted of 80 patients of whom 44 showed lominantly depressive symptoms and 14 manic

LE IV—RESULTS OF CHLORPROMAZINE IN 39 PATIENTS HAD NOT IMPROVED OR HAD RELAPSED AFTER E.C.T

sponse to E.C.T	Response to chlorpromazine				Total
	No change	Improved	Much improved	Symptom free	
o	12	4	2	1	19
ponded but peatedly re psed	4	2	9	5	20

atement 22 were considered to be predominantly rotic, and the affective disturbance was secondary environmental and other social difficulties

Table III shows that chlorpromazine was moderately cessful in controlling symptoms in simple retarded in agitated depression but had very little effect in ochondriacal depressive states and gave no very ouraging results with neurotic depressions This also our experience in treating neurotic depression outpatient clinics In contrast to Garmany et al 54) we have not found chlorpromazine of any nificant value in states of anxiety or neurotic tension in phobic or obsessional states For example of 11 s of acute anxiety states 8 showed no improvement 3 very little Nearly all our evidence however derived from outpatients not reported here in detail 0 of whom were given chlorpromazine parenterally s finding is supported by Martin (1954) and Sigwald 53) Martin (1954) comments also that patients with e conditions are often alarmed by the sensations duced by the chlorpromazine some even becoming siderably worse In view of these observations the iscriminate use of chlorpromazine in neurotic states contra indicated

Manic symptoms either responded very well or were npletely refractory and all good reactions occurred early as the first week or so A similar situation has en been observed on treating manic states with E C T., treatment being useless or even aggravating the ndition on some occasions, though producing dramatic issions on others

TABLE V—RESULTS OF CHLORPROMAZINE IN 17 MISCELLANEOUS CONDITIONS

Diagnosis	Changes in symptoms				Total
	No change	Improved	Much improved	Symptom free	
Aggressive psychopaths defectives, epileptics	4	2	0	0	6
Carcinoma pain	1	0	0	0	1
Mastectomy with mania	0	1	0	0	1
Overactive senile and presenile dementias	2	1	2	0	5
Huntington's chorea (3) undiagnosed dyskinesia (1)	[illegible]	1	1	0	4

The response to chlorpromazine by depressed patients who had not improved with E C T or had repeatedly relapsed is of considerable interest (table IV)

It will be seen that patients who had failed to respond to E C T did equally badly when treated with chlorpromazine but those who had responded to E C.T and had pursued a relapsing course did on the whole remarkably well

How long to continue the administration of chlorpromazine in depressive states is not easy to answer Some patients appear to be kept going by its use until a natural remission occurs, but most of them relapse when it is discontinued, and this particularly applied to those who relapsed on the discontinuation of E C T and were maintained by the administration of chlorpromazine

Depressed patients in whom agitation was predominant and who received chlorpromazine alone showed only a partial response similar to that seen in schizophrenic states, suggesting that the agitation and restlessness had merely been masked. In depressive or manic illness the drug is clearly no substitute for convulsion therapy but it is a useful adjunct in the initial stages when the patient is overactive and unmanageable

Miscellaneous Group

This group contains the least successful of the patients treated. The numbers in each section are, however, too small for statistical assessment (table V)

The poor effect of chlorpromazine on aggressive psychopaths, defectives, and epileptics is as might be expected, more akin to our results in neurotic tension states than in psychotic aggressiveness and tension

Benefit from chlorpromazine has been reported in a case of Huntington's chorea (Azima and Ogle 1954) Only 1 of our patients with this condition showed a slight diminution in the intensity of her movements and her mental state remained unchanged; but the patient with undiagnosed dyskinesia, possibly a case of torsion dystonia was much improved The movements were well controlled by chlorpromazine and reappeared on the substitution of a placebo

GROUP B

As already mentioned this group comprised 48 female inpatients showing motor restlessness, psychomotor agitation and excitement who were by random selection

TABLE VI—RESULTS OF TREATING 24 OVERACTIVE PATIENTS WITH CHLORPROMAZINE TABLETS AND 24 SIMILAR PATIENTS WITH PLACEBO TABLETS

—	Changes in symptoms				Total
	No change	Improved	Much improved	Symptom-free	
24 patients given chlorpromazine	8	13	1	0	24
24 patients given placebo	19	5	0	0	24

given either chlorpromazine or placebo tablets Most of them were chronic patients of poor prognosis (mean duration of stay 9 6 years, mean age 43) The aim of this investigation was to determine whether chlorpromazine was effective enough to warrant continued assessment of the larger group, and, though the results obtained from this series of chronic cases might not be applicable to the group as a whole, we felt that a positive result would warrant a bigger investigation Table VI indicates that chlorpromazine proved highly effective in the control of agitation and excitement

These results show in the patients given chlorpromazine 8 failures and 16 improvements, and in the patients given a placebo 19 failures and 5 improvements These results are significant at the better than 1% level ($\chi^2 = 11$ 5, $P<0$ 01) indicating that the drug was responsible for the benefit, because the other conditions were standardised

Complications

Previous workers have commented on the high incidence of minor fainting attacks, headaches, vague cramps, dryness of the mouth, and transient pyrexia This was our experience also, these symptoms being so common that eventually they were not recorded After a few days' treatment the patient usually made no further complaint and treatment was continued satisfactorily

Of the 224 patients 22% developed sufficiently severe complications to stop treatment, but in 10 it was subsequently restarted without further complications Major symptoms occurring either alone or in combination were severe collapse (9), persistent pyrexia (8), persistent pains in the legs or in the abdomen (7), persistent rashes (4), gross confusion (4), severe headache (4), jaundice (3), vomiting (3), severe nausea (3), persistent tachycardia (3), constipation (3), convulsions (2), facial œdema (2), parotitis (2), severe cyanosis of the legs and trophic ulcers (2), marked depression (2), cardiac failure and œdema of the ankles (2), auricular fibrillation (1), diarrhœa (1) and hæmatemesis (1)

Some of these complications require a few words of comment The convulsions occurred in 2 epileptics who had not experienced seizures for several years and were not taking anticonvulsants regularly The mechanism of the effects on the periperal circulation and the heart is not clear and would repay further investigation No case of blood dyscrasia was noted in this series, in which the longest time of administration has been over fourteen months

2 patients developed cardiac enlargement with œdema of the ankles One had shown no clinical signs of heart-disease before treatment, and the condition returned to normal when chlorpromazine therapy was discontinued The other had had previous, though less severe, attacks of congestive failure Cardiac failure and enlargement occurred after eighteen and three weeks of treatment respectively, the drug being given by the oral route in both cases

Deaths have been reported (*British Medical Journal* 1954) in 2 cases of liver damage and jaundice, and Lehmann and Hanrahan (1954) found slight changes in the cephalin-cholesterol tests in about 50%, and jaundice in 4%, of their cases

In our series the jaundice (3 cases) disappeared within forty-eight hours of discontinuing chlorpromazine therapy, and no evidence of liver damage was found with standard liver-function tests, including flocculation tests

Martin (1954) reported troublesome constipation and diarrhœa In our series one case of persistent constipation occurred after sixteen weeks, and the case of severe diarrhœa after three weeks' treatment

The incidence of complications (22%) in this series leads us to conclude that chlorpromazine requires careful supervision, particularly when given to outpatients Complications do not usually occur with high dosage in patients who have been having the drug for some but they most commonly arise between the first third weeks of treatment in those who have just with doses of 75–150 mg a day Complications no more frequent in patients who had started intramuscular injections

Discussion and Conclusions

Whenever a new drug is introduced into medical ment, enthusiasm or scepticism tend to obscure merits, unless its benefits are decisively clear, as i case of penicillin therapy, It is usually some time its true merits can be assessed and it can be giv rightful place in the armamentarium of treatment

Chlorpromazine is clearly not a curative drug schizophrenia its benefits are purely sympto the underlying thought disorder and other symp being masked This failure to provide a cure in sc detracts from its value as a special "sedative" resocialising agent We already have precedent this in the benefits from standard leucotomy, and masking action of phenobarbitone and other convulsants in epilepsy Whether a patient who had his major symptoms masked in this way for a time will eventually be able to maintain his improve after chlorpromazine therapy has been disconti still remains to be seen We are tempted to suggest if the patient's disturbed mental state can be "re sufficiently, he may remain well

The precise mode of action of chlorpromazine is obscure pharmacologically, but clinical observ suggests that cortical function is little affected, excitatory states are diminished and inhibitory s increased Some observers have used the term "ch leucotomy" to describe these effects, but in our exper such a term is misleading In no case have we obs *Witzelsucht*, euphoria, or loss of spontaneity or inhi such as may be observed after leucotomy, nor hav seen the peculiar quality of post-leucotomy indiffere nor personality changes, a point of some import Those patients who have done well have shown rapport and some insight into their condition, in our view tends to distinguish them from some leucotomy patients

Chlorpromazine is of considerable value with ch patients in the large mental hospital ward Pat who are a continual source of disturbance may be quiet, cooperative, occupied, and able to leave the pital for short periods of leave Their relatives new interest in their welfare, and this is a further help in their social recovery With the most distu elements of the community judiciously elim in this way, the ward atmosphere improves, and patients also become settled, socially improved, and responsive in the quieter environment Since the duction of chlorpromazine for selected cases less has been required, and there has been a reductio just over half in the quantity of sedatives issued by night staff Improved patients have shown inc in weight of up to 2 st, and, as suggested by Elk Elkes (1954), this appears to be related to their imp appetite and eating habits

In summary, chlorpromazine is of limited use a adjunct to other forms of therapy, or where the contra-indicated, and should be considered in following clinical conditions

(1) All types of psychomotor overactivity or excit with or without confusion

(2) Aggressive, noisy, restless, chronically over behaviour, to effect some social restoration with hospital environment

(3) Acute mania or catatonic states of excitement, E C T or insulin coma therapy can be started. patients in this group will probably need no f treatment

he proviso must be made, however that the drug is ensive compared with the usual sedatives, and luces a fairly large proportion of toxic effects which render it unsuitable for lengthy *administration*. It ld be wise to supervise carefully its use in outpatient rtments and in general practice It is of use only in nited group of patients and even when they appear ble for treatment not all will respond for reasons h are not clear at present When they are responsive ever it provides a form of assistance which is ualled by any other drug in our possession

Summary

he effects of chlorpromazine in 224 recent and chronic otic and psychotic patients were studied.

lorpromazine effectively controls the symptoms of homotor overactivity aggressiveness, agitation and hotic tension and is particularly valuable in the ment of chronic overactive deteriorated schizo nics, mania, schizophrenic excitement and patients are unsuited for electroconvulsion therapy or relapse an initial improvement after it.

lorpromazine is not a substitute for electroconvulsion py or other forms of physical treatment where are indicated Judiciously applied it can entirely the atmosphere in wards where aggressive and ted patients are treated.

considerable number of toxic reactions are ntered during its administration.

lorpromazine is a valuable though limited addition e therapeutic armamentarium of the psychiatrist

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REFERENCES

S N., Rea, F L. Duverney C A. Shea J Farkas J P 1954) *Med. Ann. D C* 23 245
H O H Hift, S., Solms W (1953) *Wien med Wschr* 03, 663
R., Ogle W (1954) *Canad med Ass J* 71 116
A. J W (1954) *Proc. R Soc Med* 47 407
Medical Journal (1954) ii 681
J H., Dutta, N K (1948) *Brit J Pharmacol* 3 354
nan, F H E (1954) *J ment Sci.* 100 882.
ler F (1953) *Laval méd* 18 332.
Bougeant H Lombard A (1953) *Ann méd psychol* 11 678
hl P N Fournel J Ducrot R., Kol ky M., Koetschet, P 1953) *Arch int Pharmacodyn* 92 305
Aims J F., Friend D G (1954) *Amer J med Sci* 227 561
J., Deniker P Hart J M. (1952a) *Ann méd. psychol* 110 267
— — Grasset (1952b) *Ibid* p 398
r, J W (1954) *Brit J Anæsth.* 26 357
J., Elkes, C (1954) *Brit med J* ii 560
ay G., May, A R., Folkson, A (1954) *Ibid* p 439
ann H E Hanrahan G E. (1954) *Arch. Neurol. Psychiat. Chicago* 71, 227
h, C A (1954) *Laval méd.* 19, 1070
N I (1943) *J ment Sci* 89 257
Ross, Jort R. Sánchez F (1954) *Sem J Amer med. Ass* 46 658
, J (1953) *Bull méd* 67 319
Boutlier D (1953) *Ann Med* 54 150
M., Adams, F H (1950) *Amer J Psychiat* 107 279
, J F Kielholtz P (1953) *Schweiz. med Wschr* 83 591
n, H (1954) *Rass Neurol veg* 4-5 211
elman, N W Jun (1954) *J Amer med. Ass* 155 18

Owing to modern conditions—lack of funds lack of and not least lack of suitable paid help—most mothers reed to look after their young children themselves. If hildren are born into an intelligent family the mother robably expect too much of them too soon—and where modern home will they find their childish refuge? by highly-strung super-sensitive difficult children he fashion while sleeping draughts and aspirin are a nonplace in the nursery Nannies are fast dying out but this is seemingly inevitable let us not therefore assume or our children are better off without these simple but people Self-expression sensible toys and lots of grated are all very well but there is more childish comfort to hand in a hand-dressed teddy and a milk pudding —LA M. L. CHANCE, *Observer*, May 22 1955 p 13

CŒLIAC DISEASE

THE RELATIVE IMPORTANCE OF WHEAT GLUTEN

CONSTANCE A. C ROSS
M.D Glasg
RESEARCH FELLOW

A C FRAZER
M.D Birm. D.Sc Lond, F.R C P
PROFESSOR OF PHARMACOLOGY

J M. FRENCH
M.D Birm. Ph.D
LECTURER IN PHARMACOLOGY

J W GERRARD
D.M Oxfd M.R C.P
LECTURER IN PÆDIATRICS

H G SAMMONS
Ph.D Birm.
LECTURER IN PHARMACOLOGY

J M. SMELLIE
O B.E., T D., M D Edin, F.R.C.P
PROFESSOR OF PÆDIATRICS AND CHILD HEALTH

UNIVERSITY OF BIRMINGHAM

From the Departments of Pharmacology and of Pædiatrics and Child Health University of Birmingham

FOR many years the term "cœliac disease" was used to describe a disorder of childhood in which chronic diarrhœa steatorrhœa and malnutrition were presenting symptoms Until recently no precise definition of this disease was made and it was generally described by various signs and symptoms Steatorrhœa was recognised as one of the most constant findings but the steatorrhœa of cœliac disease was not clearly differentiated from that of pancreatic insufficiency until Andersen (1938) separated fibrocystic disease of the pancreas as a separate entity and showed that the steatorrhœa in fibrocystic disease resulted from deficiency of pancreatic lipase. This work led to subdivision of the cœliac syndrome into *cœliac disease and fibrocystic disease of the pancreas* Further progress in the ætiology of cœliac disease was achieved when Dicke (1950) and Weijers and van de Kamer (1950) demonstrated that children with cœliac disease recovered when wheat and rye flours were excluded from their diets Subsequently it was shown that the gluten fraction of wheat and of rye contained the harmful substance and that the starch fraction was harmless to these children (Anderson, Frazer French Gerrard Sammons and Smellie 1952 van de Kamer et al 1953) The fact that not every patient with chronic steatorrhœa and normal pancreatic function responds to a wheat gluten free diet has been stressed in previous reports—in children and adolescents who received treatment late in their illness (Gerrard Ross and Smellie 1955), and in adults with idiopathic steatorrhœa (Anderson Frazer French Hawkins Ross and Sammons 1954)

The purpose of the present study was to determine what proportion of children presenting with active cœliac disease responded to a diet free from wheat gluten (rye is not a common food in this country) and to examine the ætiology of the disorder in those children who did not respond

Materials and Methods

As steatorrhœa is generally accepted as the most constant finding in cœliac disease, the main criterion for inclusion in the present series was the presence of chronic steatorrhœa with normal pancreatic function Moreover it was thought that an assessment of steatorrhœa by fat balance studies afforded the most reliable single test of gastro intestinal function Steatorrhœa was defined as a mean daily fæcal fat of over 5·0 g this was found in 30 children with normal pancreatic function aged from 6 months to 10 years, who were admitted to Birmingham Children's Hospital during the years 1951 to 1954 A marked improvement in fat absorption was the main criterion of response to the diet.

The following investigations were carried out (*a*) before treatment with a wheat gluten free diet and (*b*) after a period of from three to twenty four months on the diet:

Fæcal fat—A fat balance was carried out on each child for ten days. The child received a known dietary fat intake and the fat content of the stools was estimated daily by the fatty acid method of van de Kamer et al (1949) The mean daily fæcal fat output by each child was then calculated

Systemic lipæmia was studied by means of the chylomicrograph technique (Frazer and Stewart 1939) after a meal containing 10–20 g of fat, depending on the age of the child The actual procedure used has been previously described (Ross 1955) The maximum chylomicron increment—i e, the greatest increase in fat particles per standard high-power field above the fasting level—was obtained for each patient In this study the counts were made by two of us whose counts roughly tallied three counts were made on each blood specimen and the average count obtained As there was considerable subjective deviation in any one count, we have placed the results of the maximum increments in four broad groups—under 50, 50–100, 101–150, and 150 and over To serve as controls, chylomicrographs were carried out in 24 children, between 6 months and 11 years of age, who were not suffering from any intestinal disorder

Weights were compared with the normal standards of Engelbach (1932) as adapted by Wilkins (1950), and for each child the percentage of the standard weight for age was calculated

Glucose tolerance—Oral glucose tests were carried out in some patients, the test was omitted in children who were apprehensive or nervous The dosage of glucose was 0 5 g per lb body weight, and the blood-levels were estimated by the method of Hagedorn-Jensen

Hæmatology—In all the children, the number of red cells, the hæmoglobin value, the packed-cell volume, the mean corpuscular volume, and the mean corpuscular hæmoglobin concentration were estimated

Radiography of small intestine—The presence of dilatation of the small intestine had previously been demonstrated by means of a non flocculating preparation of barium sulphate, both in active cœliac disease (Anderson, Astley, French, and Gerrard 1952) and in the later stages of the disease (Astley and Gerrard 1954) In the present study, therefore, particular attention was paid to the degree of dilatation of the small intestine, which was classified in four groups—gross, considerable, slight, and borderline

Pancreatic enzymes—The amylase, lipase, and trypsin activities of duodenal juice were estimated (before treatment only) by the methods described by Anderson, Frazer, et al (1952)

Results

Of the 30 children 28 responded to the diet, as evide by a considerable decrease in fæcal fat (table I). Be treatment with the diet, the mean daily fæcal fat ex by each child was 6 0 g or over, the mean value for 28 children was 9 3 g (S D ±2 97) After treatment periods ranging from four to twenty four months (7 1 months) the daily fæcal fat output by each chil fallen below 5 0 g, the mean value for the 28 chi was now 3 3 g (S D ±0 97)

In order to prove that wheat gluten was inde causative factor in the children who responded to diet, wheat gluten in a dosage of 10 g daily was give the recovery stage to 12 of these 28 children, developed steatorrhœa in two to four weeks, accomp by other signs and symptoms of deterioration deterioration was as great in the children who had on the gluten free diet for many months (longest p forty eight months) as in those who had received gluten-free diet for only a few months

CHILDREN RESPONDING TO THE DIET

Chylomicrograph—It will be seen from table II th maximum chylomicron increment above 100 par was found in 10 of the 28 children before treat compared with 20 out of 24 children after treat This difference is statistically significant (P=0·001) is in agreement with the previous chylomicro findings of Anderson, Frazer, et al (1952) Althoug chylomicrograph, before treatment, was depressed majority of the children in the present series, som counts similar to those obtained in the 24 "norma 22 of the "normals" had maximum increments ove

Weight—Before treatment, all the children below standard weight for age, the figures r between 48% and 99%, with a mean of 75% Trea resulted in a substantial increase in weight, the fi at the time of reassessment ranging from 68% to 1 with a mean of 92% 8 children were then over st

TABLE I—DETAILS OF INVESTIGATIONS (A) BEFORE AND (B) AFTER TREATMENT

Patient	Age (yr and month)		Period on wheat-gluten free diet (mos)	Mean fæcal fat (g per day)		Maximum chylomicron increment		Percentage weight for age		Glucose tolerance (maximum increment in mg per 100 ml)		Hæmoglobin (g per 100 ml)		Dilatation of small intestine
	A	B		A	B	A	B	A	B	A	B	A	B	A
1	0 6	0 10	4	6 6	3 2	114		54 5	95 0			12 1		Not done
2	0 9	1 2	5	11 7	1 2	111		70 5	101 0			14 4	10 1	+++
3	0 11	1 3	4	13 8	2 1	29	150 +	88 5	97 0			11 0	11 2	++
4	0 11	2 11	24	9·0	4 2	12	81	96 0	97 5	18		14 0	12 5	+++
5	1 3	1 9	6	9 8	2 1	80	111	53 5	82 5	36		11 9	13 1	+++
6	1 7	2 2	7	6 6	3 6	150 +	150 +	67 0	83 0			8 8	13 1	++
7	1 8	2 2	6	10 0	2 4	60	150 +	70 0	77 0	30	11	8 2	12 6	++++
8	1 10	2 1	3	6 9	3 0	150 +		99 0	120 5	9	55	10 6	11 2	+++
9	2 2	3 1	11	6 0	3 0	150 +	150 +	77 0	95 5	21	42	9 6	12 6	+++
10	2 5	3 5	12	10 4	3 2	130	150	66 0	85 0	26	98	10 4	13 3	++
11	2 11	3 10	11	15 2	4 0	55	128	47 5	110 5	34	37	9 6	11 0	++++
12	3 3	4 6	15	12 0	3 2	40	175	66 0	103 0	23	45	11 8	13 3	++++
13	3 3	3 6	3	7 4	3 4	59	125	76 0	85 0	23		7 4	10 4	++
14	3 4	3 8	4	16 2	4 7	150 +	122	82 0	88 0	9	39	11 8	13 4	++++
15	3 5	4 0	7	6 5	3 5	90	150 +	85 0	100 0	66		8 9	12 7	+++
16	3 8	4 2	6	7 6	4 5	75	85	84 5	103 0	32	44	10 0	13 2	++
17	3 8	4 0	4	8 0	2 4	134	150	62 0	68 0	26		10 9	11 8	+
18	3 9	4.3	6	7 9	4 5	109		50 0	94 0			7 4	9 2	Not done
19	4 6	4 9	3	6 8	3 6	86	150 +	83 0	97 0			11 6	10 0	+++
20	5 5	5 8	3	9 5	3 3	93	150 +	71 0	77 5	34	71	11 0	10·0	+++
21	5 10	6 1	3	6 4	1 4	61	117	92 0	97 5	31	36	11 8	11 8	+
22	6 0	8 0	24	8 0	3 0	57	150	85 0	80 0	26	35	9 6	10 9	+++
23	6 5	6 8	3	6 0	4 0	64	45	96 0	102 0	25		14 0	12 6	+++
24	7 0	7 3	3	11 3	4 8	30	131	78 0	92 0	41		7 8	10 1	+++
25	7 2	7 7	5	7 0	2 0	150 +	150 +	74 5	88 5	7	63	9 6	12 6	++++
26	7 8	8 0	4	12 0	4 5	47	77	90 0	92 0		68	7 4	11 8	+++
27	9 10	10 3	5	9 9	3 3	34	135	64 0	76 0			9 4	12 4	+++
28	10 3	11 0	9	14 0	4 5	40	150	69 0	77 0	34	13	9 6	14 2	+ – – –
Means			7 1	9 3	3 3			74 9	92 0	27 5	46	10 0	11 9	
29	3 3	4 9	18	17 5	17 5	15	25	85 5	86 5	71	93	12 5	14 0	+++
30	1 7	1 8	1	8 0	8·0	36	59	115 0	115 0	47		10 7	10 7	–

• + + + +, gross + + +, considerable + +, slight +, borderline –, nil ght for age The difference in the figures before and r treatment is highly significant (P<0·001)—a ing in keeping with that obtained in a series of dren treated late in the course of the disease (Gerrard, s and Smellie 1955)

lucose tolerance.—Table II shows that, of the 20 dren who had glucose tolerance tests before treat t only 2 showed an increment above 40 mg per ml (40 mg is the minimum increment usually pted as normal) compared with 8 out of 14 tests r treatment This difference is not statistically ficant, but the number of cases in this investigation small

ematology.—As we wished to find out if the anæmia ld improve with the diet alone the majority of the dren did not receive oral iron between the two assess its. Before treatment, the mean hæmoglobin value was per 100 ml the values were below 10 g in 13 of the hildren and the anæmia was always hypochromic. reassessment the mean hæmoglobin was 11 9 g and e of the children then had a value below 10 g hough the difference between the figures before and r treatment is statistically significant (P=0 001) the oglobin even after treatment was still below 13 g 0 of the children This suggests that treatment with diet alone was often insufficient to restore the hæmo in to normal—probably because body stores of iron e low Subsequent administration of oral iron lted in a rapid increase in hæmoglobin to normal es

adiography of small intestine.—Before treatment 26 ents received a barium meal examination, with a non ulating suspension of barium sulphate 24 of these wed slight considerable or gross dilatation of the ll intestine compared with 10 out of 22 examined r treatment This difference is statistically significant 0 001) These radiographic findings agree with those rted by Anderson et al (1952) and Astley and ard (1954)

onclusion.—In this group of 28 children who responded wheat gluten free diet as shown by a decrease in l fat the results of most of the other investigations wed a concomitant return to normal values Thus, e was a highly significant increase in standard weight age, and a significant rise in the maximum chylo ron increment and in the hæmoglobin level There also a significant diminution in dilatation of the ll intestine The increase in the maximum increment he glucose tolerance test was not however statistically ificant

CHILDREN NOT RESPONDING TO THE DIET

n 2 cases there was no decrease in fæcal fat

e of Bile-salt Deficiency

ase 29.—This girl was admitted for investigation when 3 s old Her mother stated that she had passed bulky ish stools since the age of 2 months and had had several cks of bronchitis. She was an active child with a good etite Table I shows that at this time she had a fæcal fat put of 17 5 g per day a flat chylomicrograph a percentage ght for age of 85 5 a normal glucose-tolerance test, a noglobin level of 12 5 g per 100 ml and considerable tation of the small intestine The duodenal juice contained pancreatic enzymes, amylase lipase and trypsin in mal amounts

he was treated with a wheat gluten free diet, but after teen months there was still no improvement in the torrhœa. She was then placed on a fat free diet and the content of her stools immediately fell to 3–4 g per day hich is within normal limits. This indicated that the fæcal was largely of dietary origin and that the steatorrhœa was related to the ingestion of wheat gluten

t 3½ years old her general condition was good, but the torrhœa was unchanged; the chylomicrograph was still even after an oral feed of emulsified olive oil buffered in n milk. Serum-cholesterol 105 mg per 100 ml (free 48 mg) serum bilirubin 0·2 mg per 100 ml bromsulphalein and thymol turbidity tests normal serum alkaline phosphatase 20 King Armstrong units

In view of the finding of steatorrhœa with normal pancreatic lipase and lack of response to a wheat-gluten free diet it was thought that this child might have a deficiency of bile salts. She was therefore given a preparation of bile Desibyl capsules gr 10 thrice daily half an hour before meals. Within a week her fæcal fat had fallen below 10 g per day and it remained between 4 g and 12 g daily while she received bile After six weeks the bile was discontinued and her fæcal fat output rose immediately to the original levels (see figure) Bile was recommenced and the child was discharged home. At the end of eleven months the bile was discontinued and she was given a low fat diet.

At the age of 7 she was readmitted to hospital for review having been six months on this low fat diet Her general condition remained good the chylomicrograph was still flat, even after emulsified olive oil. A barium meal with a non flocculating preparation of barium sulphate showed slight dilatation of the small intestine; when the examination was repeated with the same barium preparation with the addition of 10% butter there was no difference in the transit time. Serum-cholesterol 281 mg per 100 ml (free 185 mg)

TABLE II—RESULTS OF INVESTIGATIONS IN CHILDREN RESPONDING TO A WHEAT-GLUTEN FREE DIET (A) BEFORE AND (B) AFTER TREATMENT

FÆCAL FAT

—	Total	No of patients with mean fæcal fat (g per day)			
		15 and over	10–14 9	5–9 9	Under 5
A B	28 28	2 0	8 0	18 0	0 28

CHYLOMICROGRAPH

—	Total	No of patients with maximum increment			
		Under 50	50–100	101–150	150 and over
A B	28 24	7 1	11 3	5 7	5 13

WEIGHT

—	Total	No of patients with percentage weight for age						
		40–	50–	60–	70–	80–	90–	100–
A B	25 *28	1 0	3 0	6 1	 1	6 7	5 8	0 8

GLUCOSE TOLERANCE

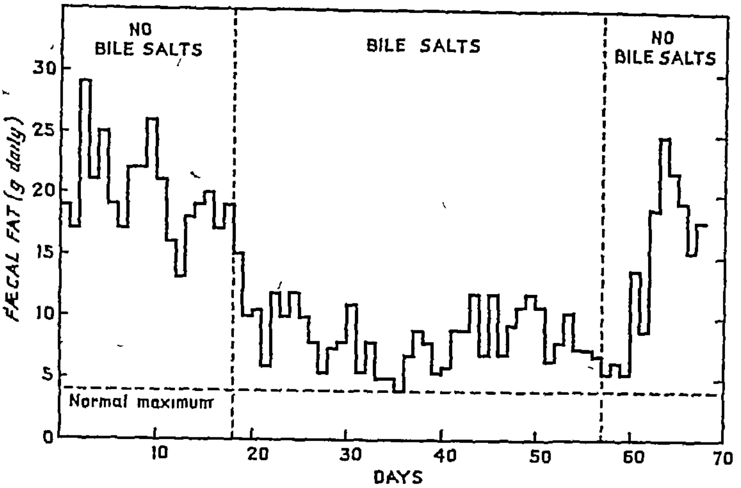
—	Total	No of patients with maximum increment (mg per 100 ml.)				
		0–	11–	21–	31–	40–
A B	20 14	3 0	1 2	8 0	6 4	2 8

HÆMOGLOBIN

—	Total	No of patients with hæmoglobin (g per 100 ml)						
		7–	8–	9–	10–	11–	12–	13–
A B	25 27	4 0	3 0	6 1	4 6	– 6	1 7	3 7

RADIOGRAPHIC DILATATION OF SMALL INTESTINE

—	Total	Gross	Considerable	Slight	Borderline	Nil
A B	26 22	6 0	13 0	5 10	2 10	0 2



Continuous fat balance in case 29, on 50 g fat daily, showing fall in fæcal fat on bile-salt therapy, followed by deterioration on withdrawal of bile salts.

On her last admission, in February, 1955, at 7½ years of age, an analysis of duodenal fluid gave the following findings alkaline phosphatase 54 K A units, cholesterol 6 5 mg per 100 ml (free 4 9 mg), Pettenkofer's reaction faintly positive The lipase activity of the fluid was determined by the method used by Anderson, Frazer, et al (1952), but two estimations were made, one with additional bile salts, as described, and one without additional bile salts The lipase activity was 2 6 units in the sample with additional bile salts compared with 1 3 units in the sample without additional bile salts, that is to say, the ratio of lipase activity in the estimations with and without bile salts was 2 1—approximately the same as that found in the duodenal juice of children without steatorrhœa

Two samples of duodenal juice were examined for cholic acid content by an adaptation of the method of Chabrole et al (1934) Table III shows that the cholic acid in these samples was respectively 0 21 mg per ml and 0 1 mg per ml—values were considerably below those obtained in specimens of duodenal fluid from 5 other children suffering from various disorders Blood serum analysis showed that cholesterol was still rather high (total 271 mg per 100 ml, free, 93 mg) The bilirubin content was 0 36 mg per 100 ml and the hæmoglobin 14 8 g

The disappearance of this child's steatorrhœa when she was on bile therapy, and the finding of a low cholic-acid content in her duodenal juice, suggest that her steatorrhœa was due to a deficiency of bile salts Despite the severe steatorrhœa, her nutrition was good, although a nitrogen balance was not carried out, it would seem that the defect in absorption mainly affected fat

Case of Fat Intolerance

Case 30.—This boy's birth-weight was 9 lb 6 oz, he was breast fed for five weeks and was then given National dried milk (half cream), and he was well until 2½ months old, when he had an attack of vomiting and diarrhœa which was diagnosed as gastro-enteritis Vomiting and diarrhœa persisted intermittently up to the time of his admission to Birmingham Children's Hospital at 4 months of age

At this time, he was marasmic (weight 8 lb 7 oz.) and so dehydrated that he required intravenous therapy No pathogens were isolated from his fæces When
valescent, he could tolerate only oral feeds
skim milk, he would vomit within half an
of receiving a feed of breast-milk, or Nat
dried milk, and subsequently had diarrhœa
could tolerate no more than 15 g. fat da
either as milk fat, margarine, or olive oil
on this dosage he had steatorrhœa his fæcal
ranging between 5 g and 9 g daily Bil
orally did not decrease the fæcal fat Estim
of amylase, lipase, and trypsin in duodenal
gave normal values He was discharged
hospital at the age of 14 months on Cow &
separated milk and a fat-free diet

TABLE III—CHOLIC ACID CONTENT OF DUODENAL JUICE

Patient	Age	Cholic acid (mg per ml)
Case 29	7 yr	(1) 0 21 (2) 0 1
Bronchitis	4 mos	2 4
Salmonella carrier	6 mos	3 1
Pancreatic fibrosis	6 mos	4 68
Bronchitis	2 yr	(1) 1 75 (2) 1 45
Cœliac disease	5 yr	(1) 1 4 (2) 1 3

When he was readmitted at 19 months of
his general condition was good (weight 2
4 oz) and he was able to tolerate 20 g fat d
but more than this provoked vomiting
diarrhœa Table I shows the results of inves
tions at this time In addition to the
micrograph after a standard fat meal,
micrographs were also carried out after
unemulsified and (*b*) emulsified olive oil,
rise in particle count was equally low in b
The serum-cholesterol was 657 mg
100 ml (free 44 2 mg)

On his last admission, at 2 years 9 months, his weight
30 lb He still had steatorrhœa and was still only ab
tolerate 20 g fat daily The serum cholesterol was 1
per 100 ml (free 81 5 mg) A barium meal was now ca
out (*a*) with fat and (*b*) without fat, using a non flocc
type of barium sulphate The examination with fat (
butter in the suspension) showed considerable gastric
with a residue in the stomach at seven hours, but no
twenty four hours, the barium in the small intestine
clumped into small aggregations, barium had reached
colon by four hours after the meal In the same examin
without fat, the stomach emptied normally, at one a
half hours, it contained only a little residue, the patt
the small intestine appeared normal The main diffe
between the examinations with and without fat was, the
the gastric inactivity in the examination with fat In a co
subject (a girl of 3 years in whom there was no reason
suspect gastric abnormality), the same amount of barium
mixture had left the stomach in two to three hours.

This child's symptoms seem to have originated from
attack of gastro enteritis in infancy The occurrence
vomiting after a meal containing a moderate amount
fat, together with radiological evidence of gastric st
in the barium meal containing fat, suggested that
administration of fat resulted in pylorospasm The c
of the steatorrhœa remains obscure

Discussion

28 out of 30 children with signs and symptoms of ac
cœliac disease recovered on a diet free from wheat glu
As they had all been ill for several months before tr
ment, their recovery on the diet is strong evidence
favour of the ætiological relationship of wheat gl
to their illness More precise evidence of this relation
was obtained by the reappearance of steatorrhœa
reintroduction of wheat gluten into the diet of 12 of th
28 children

2 of the children in the present series failed to resp
to the diet In their reinvestigation of 34 children
cœliac disease Gerrard et al (1955) likewise found 2
did not respond It therefore seems that, in a few ca
factors other than wheat gluten may be responsible
signs and symptoms of cœliac disease

In 1 of our 2 children the cause appeared to
deficiency of bile salts, and it is of interest that this
been proposed in the past as a possible cause of cœl
disease (Cheadle 1903, Miller 1920, Macrae and Mo
1931) Macrae and Morris demonstrated that in some ca
oral administration of bile salts improved fat absorption
either (they thought) because it made good a deficie
or because bile salts aided absorption of soaps. Th
present study suggests that a specific deficiency of b
salts may occasionally be responsible for steatorrhœa

n the other child who did not respond to the diet the ptoms of 'fat intolerance' dated from an attack gastro-enteritis A similar case also originating in tro-enteritis in infancy, is included in the series of rard et al. (1955) When last seen at 7 years old their d was still unable to tolerate fat if given 30 g fat y she had frequent vomiting with steatorrhœa In connection it is worth noting that after gastroentis the reintroduction of fat into an infant's feeds n needs to be gradual It would appear that these hildren had not regained their ability to assimilate

hough our findings show that various factors can give to the clinical picture of cœliac disease the vast nty of the children in our series—who had chronic torrhœa with normal pancreatic function—responded diet free from wheat gluten It now seems appro te to consider this disorder as a separate entity for h the term gluten induced cœliac disease' is gested.

Summary

f 30 children with active cœliac disease all but 2 onded to diets free from wheat gluten The main nostic criterion was chronic steatorrhœa with normal creatic function; and the main therapeutic criterion disappearance of the steatorrhœa

n the children who recovered on a wheat-gluten free improvement in fat absorption coincided with rovement in chylomicrograph standard weight for and hæmoglobin level, and with diminution in the dation of the small intestine but not with any ificant improvement in the glucose tolerance test

f the 2 children who did not respond to the diet 1 eared to have a deficiency of bile salts and the other d showed fat intolerance.

he term ' gluten induced cœliac disease is suggested the disorder in those children who recover on diets from wheat gluten

e wish to thank the consultant staff of the Children's pital Birmingham, for permission to study their patients, Sister N Howells and Sister J Woodward for invaluable with the metabolic studies. We are grateful to Dr otte Anderson for the results with earlier cases, to Dr R ky for the radiographic assessments and to Dr J A H. terhouse for the statistical analyses. We are indebted to J Kemp and Miss M Cutler for technical assistance ally we gratefully acknowledge financial assistance from United Birmingham Hospitals Research Fund and the ical Research Council.

REFERENCES

kren D H (1938) *Amer J Dis Child* 56 311
rson, C M, Astley R French J M, Gerrard J W (1952) *Brit J Radiol* 25 526
Frazer, A C, French J M, Gerrard J W Sammons H G Smellie J M (1952) *Lancet* i 836
— — Hawkins, C F Ross C A C Sammons H G (1954) *Gastroenterologia* 81 98
ey R, Gerrard J W (1954) *Brit J Radiol* 27 484
and F Charnnat, R, Cottet J Blondet I (1931) *C.R Soc Biol, Paris*, 115 834
dle W H (1903) *Lancet* i 1497
ke W K (1950) Coeliakie Utrecht M D thesis
tibach W (1939) Endocrine Medicine Springfield Illinois vol. II
er A C Stewart H C (1939) *J Physiol* 95 211 73P
rard J W Ross C A C Smellie J M (1955) *Lancet* i 587
ne O Morel N (1931) *Arch. Dis. Childh* 6 75
r R (1950) *Lancet* ii, 1166.
e C A C (1955) *Arch Dis Childh* (in the press)
de Kamer, J H, ten Bokkel Huinink, H Weijers H A (1949) *J biol Chem* 177 347
Weijers H A Dicke W K (1953) *Acta pædiat Uppsala* 42
ers H A, van de Kamer J H (1950) Fat Absorption in Normal and Abnormal Infants and Children with Special Reference to Cœliac Disease Centraal Inst r Voedingsonderzoek T.N.O publication no. 113 Utrecht
kins L (1950) The Diagnosis and Treatment of Endocrine Disorders in Childhood and Adolescence Springfield Illinois

HIGH-PRESSURE OXYGEN AND RADIOTHERAPY

I Churchill-Davidson
M.A M.B Camb D.M.R T
ASSISTANT RADIOTHERAPIST

C Sanger
M.B Lond. F F.A.R.C.S
SENIOR REGISTRAR IN ANÆSTHETICS

R H. Thomlinson
M.A. M B Camb
ASSISTANT CURATOR PATHOLOGICAL MUSEUM

ST THOMAS'S HOSPITAL, LONDON

A PRELIMINARY investigation has been made into the effects of irradiating carcinomata in patients breathing oxygen at a pressure of three atmospheres absolute (30 lb per square inch gauge pressure) This was suggested by the findings of Gray et al (1953) who showed that the sensitivity of tumour cells to irradiation was increased in mice breathing oxygen

It appears to be a general principle that the sensitivity of all cells to irradiation is related to the oxygen concentration in their environment This sensitivity increases rapidly as the oxygen concentration increases to a critical level above which there is little further change

Evidence has been obtained from the structure of neoplasms that they contain cells which in relation to those of normal tissues are in a poor state of oxygenation (Thomlinson and Gray 1954, 1955) An increase in the concentration of oxygen around these cells would therefore cause a relatively greater increase in their sensitivity to irradiation

This encouraged us to investigate the possibility of improving the treatment of patients Firstly we considered the physiological and technical problems involved To reach a pressure of three atmospheres a pressure chamber is required Exposure to oxygen at high pressure for more than short periods is liable to cause convulsions (Bert 1878 Thomson 1935 Donald 1947 Lambertsen et al 1953) In animals, however the onset of convulsions can be retarded by barbiturate anæsthesia (Marks 1944 Taylor 1954 Churchill Davidson 1954) We have therefore anæsthetised our patients before the administration of oxygen They were thus not susceptible to alarm at being enclosed in the chamber or to the severe pain which is sometimes felt in the paranasal sinuses in atmospheres of high pressure

Because of the possibility of extensive rupture of the tympanic membrane or hæmorrhage in the middle ear bilateral myringotomy was done Small polyethylene tubes such as have been used in the treatment of chronic secretory otitis media (Armstrong 1954) kept the perforations patent during treatment

It is impossible to remain in the same room as the pressure chamber during irradiation but contact with the patient can be maintained electrically We have used an electrocardiograph an electromyograph from the upper lip to detect the possible onset of convulsions and a thermistor mounted on the outlet of a carbon dioxide absorbing canister to obtain a tracing of the respiratory rate Special precautions were necessary to avoid static or other sparking because of the risk of fire or explosion

We used a modified naval diving recompression chamber (fig 1) This consists of a steel cylinder measuring internally 7 ft 6 in × 2 ft 6 in with a door at the head and secured by swing bolts It is mounted on four swivel wheels and can be moved by two people although it weighs two tons There are two observation ports in the door and on top of the chamber is a recessed window 25 cm sq of 1 in Perspex through which the patient is irradiated At the foot end of the chamber is an inlet manifold connected directly to four 120 cu ft oxygen

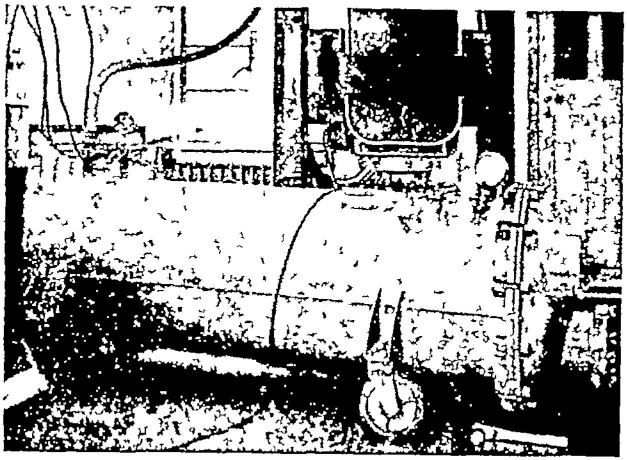


Fig 1—Pressure chamber in position under X-ray unit

cylinders without reducing valves A pressure gauge is attached to the manifold There are also a safety valve and a $1^1/_2$ in exhaust valve from which the oxygen is discharged from the building through a hose pipe At the head end of the chamber are a gauge measuring the pressure within the chamber, a fine needle exhaust valve, and a second safety valve Inside the chamber is staging on to which slides a metal trolley carrying the patient To get this easily in and out of the chamber a second trolley has been made on to which the first slides (fig 2) The electrical leads pass out of the chamber through a pressure gland and are connected via twin amplifiers to a double-beam cathode ray tube One beam is used to make the tracing from the thermistor and the other to make a combined tracing from the electrocardiograph and electromyograph A second cathode ray tube and camera enable these tracings to be photographed (fig 3)

The radiotherapy apparatus is a standard 250 kV unit filtered to give a half-value layer of 1 70 mm of copper (in treating one of the breast tumours—case 6—this was reduced to 1 15 mm to get a higher dosage rate)

To obtain results quickly we tried to determine whether the expected increase in radiosensitivity was demonstrable histologically To do this we treated patients with carcinomas large enough to be divided into two fields for irradiation One field was irradiated with the patient breathing air at atmospheric pressure, and the other with the patient breathing oxygen at three atmospheres in the pressure chamber Each field was irradiated once only with the same dose of X rays To compare the effect on

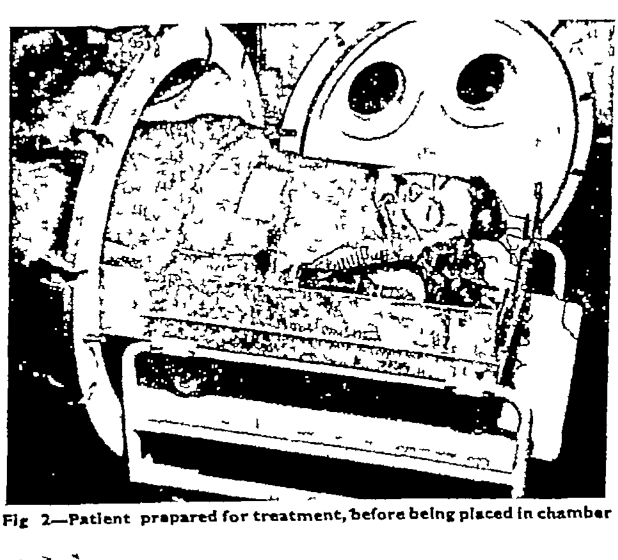


Fig 2—Patient prepared for treatment, before being placed in chamber

the two fields a dose was given (1000–1500r at the which was insufficient to kill all the cells After an a biopsy specimen was taken from each field, or growth was excised, and the pathologist was told the dividing line between the fields lay but not field had been irradiated in oxygen

Eight patients were treated four had carcino the lung, and four carcinomas of the breast (two local recurrences after mastectomy) The breast were treated in two anterior fields and were divid covering one half with lead sheets

The lung tumours were treated in directly op anterior and posterior fields To obtain an ac line of division the patients were screened in the positions in which they were to be treated With patient supine a wire mesh grid was placed on the an chest wall and adjusted so that the central wire directly over the proposed line of division The grid then outlined on the skin surface with a dye so th could be replaced in the same position With the tube centred over it an anteroposterior picture was (fig 4) The whole procedure was then repeated with patient prone and the grid on the posterior chest wall, a postero anterior film was taken When the films been developed, the grids were replaced and the marked with any small adjustments necessary

Procedure

Premedication —Phenobarbitone gr 1 was given hours before treatment, and atropine gr $^1/_{\rm 0}$ 'Omnopon' gr $^1/_6$ one hour before treatment In 7 and 8 chlorpromazine 50 mg and pethidine 100 were given intramuscularly instead of omnopon

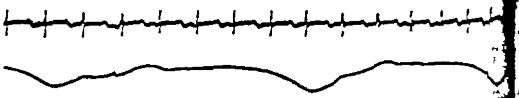


Fig 3—Electrocardiograph and breathing traces Any mov the patient s upper lip will cause an electromyograph tra superimposed on the electrocardiogram The notches in the ing trace are caused by closure of the valves

Anæsthesia and Myringotomy —Pentobarbitone in 5% solution was injected intravenously thro Gordh needle at the rate of 1 ml a minute until cons ness was lost, 0 25 g usually sufficed, but in one 0 75 g was needed Pethidine 100 mg was then slowly through the same needle, followed by choline 50 mg In cases 7 and 8 only chlorpr 50 mg was given with the pethidine The patient's were next inflated with oxygen and, after the trach vocal cords had been sprayed with 4% lignocaine, largest convenient endotracheal tube was passed direct vision The tube was secured, and a metal of sufficient size to prevent biting of the tube was Controlled respiration was applied until sp breathing returned, this was done with 75% oxide and 25% oxygen while the myringotomies performed The anæsthetic machine was then nected and the patient allowed to breathe air

Preparation for Treatment —At this stage the was transferred to the pressure-chamber trolley, carbon-dioxide absorber was connected, and the trodes were applied to the left leg, upper lip, and arm To confine the irradiation to one of the fields time the other field and the surrounding skin covered with lead sheets 2 mm thick (or thickness of lead rubber), and the tube was placed its central ray passed through the middle of the di line When the patient had been correctly placed chamber, the height of the X ray tube was adju that the anode skin distance was 60 cm, and the ele connections were completed

Compression —Before the door was closed the ch was flushed with oxygen to wash out the air The es were closed oxygen allowed ow into hamber ll the uired ure was ched pression carried fairly wly to nimise bon di le reten n (Bean 5) and perature anges bout 10 nutes ally be allowed Treatment l Decom- ssion — eatment bk on average 40 minutes for each field After this the ent was slowly decompressed In the patients with ast tumours this took about 7 minutes. It could bably be done in less time because bends' (caisson ase) rarely occur with oxygen, but excessive cooling the patient might occur Decompression of patients h lung tumours was done more slowly taking about minutes This was because of the risk of damage to lung beyond a partially blocked bronchus by oxygen aining at a higher pressure

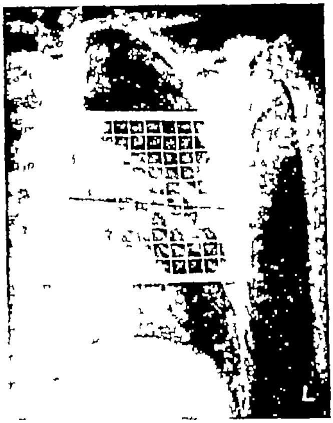


Fig 4—Anteroposterior radiograph showing wire-mesh localising grid in position. The dark line across the grid is that about which the tumour was divided into two irradiation fields.

Case reports

ase 1 —A woman aged 40 had an extensive carcinoma he left breast, which was swollen hard and fixed There e multiple nodules in the overlying skin and erysipeloid ltration extending wide of the breast in all directions. arged fixed glands were present in the left axilla and supra vicular region. The left arm was dusky and swollen and re were engorged veins around the shoulder

reatment —The breast region was divided transversely t above the nipple into two irradiation fields. The upper d was the larger having an area of 330 sq cm. and included cervico-axillary lymph chain The lower field was 120 sq A single dose of 1000r was given to each area, the upper d being irradiated with the patient breathing oxygen at e atmospheres and the lower field four days later with patient breathing air at atmospheric pressure

esult —The skin reaction in the field irradiated during the alation of oxygen was slightly more than that in the field diated in air There was dramatic regression of the tumour both fields but clinically there was little difference between m. As swelling diminished the primary tumour was nd to be in the upper and outer quadrant of the breast— wholly in the field irradiated in oxygen.

iopsy of each field 14 days after treatment showed skin a little subcutaneous tissue There was lymphatic ation of the dermis but few tumour cells were present in er specimen In the tissue irradiated in air there were e undamaged tumour cells than in the tissue irradiated oxygen, in which there was also more inflammatory ponse

ase 2 —A man, aged 61 developed a recurrence of carcin a of the left breast beside the scar of a radical mastectomy e two years previously It measured 73 × 67 mm was d to the chest wall and was fungating through the n. Lying lateral to it separated by about 20 mm of appar ly healthy skin was a nodular skin recurrence 10 mm. diameter In addition there were another skin nodule 7 5 mm in diameter in the medial infraclavicular region and small fixed glands in the left axilla and supraclavicular region

Treatment —The main mass was divided diagonally into two irradiation fields, and each was given a single dose of 1000r One was irradiated with the patient breathing oxygen at three atmospheres, and the other two days later, with the patient breathing air at atmospheric pressure The skin nodule lateral to the main mass was treated in oxygen simultaneously with the first field.

Result —Striking regression of the main mass resulted but there was little difference in the flattening of the two halves or in the skin reactions

Biopsy specimens were taken from apparently comparable areas of each field 16 days after treatment These consisted of skin and subcutaneous tissue with large numbers of tumour cells in the dermis. In the tissue treated in oxygen a higher percentage of tumour cells had been damaged and there was a greater inflammatory response In the tissue treated in air there were undamaged cells and a few in mitosis.

Skin Nodules —The skin nodule treated in oxygen had completely disappeared 14 days later For comparison the nodule in the infraclavicular region which had not been treated was allowed to reach a diameter of 10 mm and then given a single dose of 1000r in air Three weeks later it had shown only slight regression, then being 8 mm in diameter

Case 3 —A man aged 48 had a large mass in the hilar region of the left lung The left upper lobe bronchus on tomography appeared to be completely blocked and the lower lobe bronchus narrowed This was confirmed by bronchoscopy

Treatment —The growth was treated in one session each half receiving a minimal tumour dose of 1000r from opposing 8 × 15 cm. fields. The lower half was treated with the patient breathing air and one hour later the upper half with the patient breathing oxygen at three atmospheres.

Result —On radiography one and two weeks after treatment there appeared to be a dramatic regression of the tumour. The skin reaction was more marked in the field treated in oxygen but the difference was not great Three weeks after irradiation a left pneumonectomy was done No difficulty which might be considered due to irradiation was experienced.

Operation Specimen —The tumour was an oat-cell carcinoma arising in the upper lobe bronchus With the exception of a few tumour cells in a lymph node in the hilum all the cells in both fields appeared to be necrotic

Case 4 —A woman aged 53 had had a radical mastectomy for carcinoma of the right breast No postoperative irradiation was given. For nine years she remained clinically free from recurrence but then began to develop multiple local skin nodules and later glandular metastases These were treated as they arose some surgically and others by irradiation Thirteen years after the mastectomy she developed two skin nodules, each 7 mm in diameter 20 mm. apart in previously unirradiated skin

Treatment —A single dose of 1500r was given to each nodule one with the patient breathing air and the other about half an hour later with the patient breathing oxygen at three atmospheres.

Result.—Three weeks later there appeared to be slightly more regression of the nodule treated in oxygen, but the difference was not sufficient to be conclusive There was no difference in the skin reaction in the two areas. The nodules were then excised

Histology —In each nodule there were areas of tubular cuboidal and columnar cell carcinoma and no damaged tumour tissue was present It appeared from serial sections that active growth was taking place in each nodule but to a lesser extent in the one treated in oxygen in which there were also more chronic inflammation and fibrosis

Case 5 —A man aged 59 had a large mass in the lower lobe of his right lung It was found on bronchoscopy that the basal branches of the lower lobe bronchus were completely obstructed by a tumour This was a poorly differentiated squamous carcinoma.

Treatment —The growth was divided diagonally into two irradiation fields of equal size The lower and inner area was treated with the patient breathing air about an hour later the upper and outer area was treated with the patient breathing oxygen at three atmospheres Each area received a minimal tumour dose of 1000r from opposing triangular fields 15 × 15 × 21 cm

Result —Radiography 12 days after treatment showed no regression Sixteen days after treatment a right pneumonectomy was done

Histology —The tumour was approximately spherical and 8 cm in diameter It occupied most of the lower lobe of the lung and infiltrated the diaphragm and pericardium But for an incomplete rim of carcinoma 1–3 mm wide the whole mass was necrotic In this rim there appeared to be more irradiation damage in the upper and outer area

Case 6 —A woman, aged 57, had a firm tumour measuring 7 5 × 6 cm in the lower outer quadrant of the right breast This was fixed to the overlying skin, in which there was a small ulcerated area, and to the underlying muscle There was also extensive infiltration of the surrounding skin

Treatment —The tumour was divided into two fields for irradiation in a sagittal plane The lateral field, which measured 10 × 15 cm , was irradiated with the patient breathing air About an hour later the medial field, which measured 12 5 × 15 cm , was treated with the patient breathing oxygen at three atmospheres A single dose of 1500r was given to each area Owing to the rounded contour it was impossible to avoid a small area in the centre of the main mass receiving irradiation from both fields, but this was minimised by leaving a gap of 1 cm between the adjacent edges of the two fields

Result —A local mastectomy was done 10 days after irradiation At this time there was no obvious regression in either half of the tumour, and the skin reaction, a mild erythema, was similar in each irradiation field

Histology —The main tumour mass measured about 3 × 3 cm , and 1 5 cm between the retracted skin and muscle It was an acinar polygonal cell carcinoma in which a few tubules lined by columnar cells had been formed There was extensive infiltration of the dermis beyond the main mass The most severe damage caused by irradiation had occurred in the primary tumour close to the dividing line between the irradiation fields Tumour cells in the dermis in the field treated in oxygen had been damaged by irradiation There was some damage, probably less, to tumour in the region thought to have been treated in air only, but this was too near the line of division for us to be sure that it was not affected by the overlapping of the fields

Case 7 —A man, aged 48, had in the hilar region of his left lung a large mass which had obstructed the origin of the upper lobe bronchus

Treatment —The tumour was divided transversely for irradiation, each half receiving a minimal tumour dose of 1000r from opposing fields measuring 7 5 × 15 cm. The lower half was treated with the patient breathing air, and then about an hour later the upper half with the patient breathing oxygen at three atmospheres

Result —Radiographs, including tomograms, taken 11 days after treatment showed much regression of the growth but no demonstrable difference between the amounts in the two areas Thirteen days after irradiation a left pneumonectomy was done

Histology —The tumour arose in the lingular branch of the upper-lobe bronchus and measured about 25 × 15 × 15 mm There was extensive infiltration of the hilar lymph nodes, the walls of the upper lobe and lower lobe bronchi, and the adjacent lung tissue The tumour was a poorly differentiated round cell and polygonal cell carcinoma In the central portion, about the dividing line, was much necrosis In comparable fields near the upper and lower limits of irradiation was much more damage to the tumour cells in the upper part, which was irradiated in oxygen

Case 8 —A man, aged 62, had a mass in the hilum of his left lung with consolidation of much of the lung distal to it The mass was found to be a poorly differentiated squamous carcinoma

Treatment —The tumour was divided transversely for irradiation, each half receiving a minimal tumour dose of 1000r from opposing fields measuring 10 × 12 cm The lower half was treated with the patient breathing air, and the upper half about an hour later with the patient breathing oxygen at three atmospheres

Result —Radiography a week after treatment showed no mat [illegible] Ten days after treatment thoracotomy was done A large growth at the hilum was found to be ir because of extensive involvement of the aorta

Biopsy specimens were taken from the upper and halves of the growth These contained small amounts of and trabecular squamous carcinoma There appeared to more irradiation damage in the specimen from the upper

Results

Satisfactory, though experimental, apparatus and nique have been developed for the irradiation breathing oxygen at high pressures

Eight patients were treated without mishap or com cation attributable to the treatment

The pathologist was not told which part of the had been irradiated in air and which in oxygen cases (1, 2 4, 5, 7, and 8) the tissue which he to be the more damaged was that irradiated in ox This was also probably true of case 6, but the of the experiment were not fulfilled, the pathologist been told, because of some misunderstanding about dividing line, which tissue was which In case 3 distinction was made because none of the tumour either field had survived

Discussion

Empirically oxygen is known to enhance the da caused by irradiation, and, although the mechanism understood, some possibilities have been discussed (G 1953) The relation between the tension of ox dissolved in the environment of the cells and the d of damage which occurs follows a common patt plants and animals, both in vivo and in vitro G this relationship is represented by a curve rising ste from zero and then flattening out suddenly as the s tivity to irradiation almost ceases to be affected by further increase in oxygen tension During the ris sensitivity of the cells is increased by three times T this it would be expected that tissues with poor b supply would be much more affected by irradiation oxygen than would normally oxygenated tissues

Since there are areas in almost every malignant where there is necrosis caused by poor circulation, are likely to be areas of living cells in various deg oxygen deficiency It is postulated that the res of oxygen will increase the sensitivity of these cells irradiation damage and so produce a relative increase the amount of damage to the tumour as a whole compa with normal tissues As a corollary it is also postula that, if poorly oxygenated cells survive the ma doses of X rays tolerable in normal practice, they ma because of the inflammation following death of the be oxygenated tumour cells, receive a blood supply for them to continue to multiply

The work done by Gray et al (1953) on irradi during respiration of high pressure oxygen was con to plants and laboratory animals Their results sufficiently encouraging to warrant an early trial in Many investigations are being conducted with oxyge one atmosphere, and at least one encouraging rep been published (Hultborn and Forssberg 1954) We that information was urgently required about the ef of irradiation in patients breathing oxygen at atmospheres

This pressure has been used experimentally, but t is as yet no definite evidence that it is ideal in particular tumour It seems likely that different p will be required to produce the optimal results in tum with different circulatory conditions

In the treatment of our patients we have assumed Gray that, to be effective, oxygen and irradiation be administered simultaneously We are aware that it been suggested (Gerschman et al 1954) that oxygen po ing and the effects of irradiation have a mechan common, which may be cumulative even if the is breathed within a few hours after irradiation

We have explained as fully as possible the experimental ature of the treatment to each of our patients and have tained from each specific permission to do all that we tended In selecting patients for treatment care was ken to choose only those with advanced disease In es 3 5 6 7 and 8 the surgeon considered the growth be of doubtful operability, and in these the irradiation s given as a preoperative measure In cases 1, 2, and the presence of metastases made palliative irradiation only possible treatment

The apparatus we have used is experimental and has limitations for instance it is only possible to treat mours in the upper half of the body and only one field a time can be treated without decompressing and ving the patient Although the procedure has been e, it has been tedious and time-consuming, taking up six hours for a single patient This however, was tly due to our treating the tumours in two separate rations, and partly to the low output of our X ray it.

As regards anæsthesia, the main problem has been to p the patient safely anæsthetised for a long period ing which he was inaccessible to the administration of ther drugs. Pentobarbitone sodium was suitable for purpose as well as for delaying convulsions, but the essity for using an endotracheal tube to guarantee an way caused difficulty due to coughing This could not overcome by local anæsthetic or cough-depressant gs Therefore in later patients chlorpromazine has n added although it is known that this may alter ulation rates in the tissues this factor however, probably not important Chlorpromazine has the antage of being itself a protection against oxygen vulsions (Paton 1955)

The prevention of carbon dioxide accumulation in the mber is of great importance because the inhalation even small percentages of this gas accelerates the onset oxygen convulsions It is essential that all expirations passed through an absorber To avoid inspiratory istance two one way valves were used which enable patient to breathe in directly from the surrounding osphere and out through the absorber Since the nistor only gives the respiratory rate we hope in ure to get additional information by incorporating a rophone in the endotracheal tube The anæsthetic blems and technique are discussed in detail elsewhere nger et al 1955)

The anæsthetic was completely effective in preventing vulsions and no late complications were experienced patients were warned of possible slight temporary s of hearing after treatment In practice this was nimal and did not usually last more than twenty four rs. Since each patient was only treated in the pressure mber once the polythene tubes used to keep the ringotomy perforations patent were removed imme- tely afterwards If it were intended to give serial atments they could, however be left in situ for several eks without ill effect

Because of the dose given and the area treated radiation kness was anticipated Therefore dimenhydrinate mg and pyridoxine 20 mg were given three times ly for five days, and no radiation sickness developed case 7 to ascertain whether oxygen was protecting inst sickness we omitted these drugs and moderate iation sickness resulted

The difficulty of obtaining a sharp dividing line ween the two irradiation fields in lung tumours has ited us to treating comparatively large growths In te of the precautions taken we have assumed when ing biopsy specimens or examining the whole speci n that there was an area of overlap and confined our ention to areas of the tumour farthest from the ding line The whole object of the histological exam tion was to see if there was a recognisable difference between tumour tissues treated in the two different ways The main difficulty was to ensure that the areas examined were as far as possible comparable In some cases the pathologist selected the tissue irradiated in oxygen from the appearance of the tumour cells alone but in others indirect evidence such as the degree of inflammatory reaction was taken into account Because of this the reasons for the selection in any single case are open to criticism but the total result of the selections sufficiently suggests an increased effect of irradiation in oxygen to warrant a more extensive trial

It will be noted that the interval between treatment and either biopsy or excision of the tumours varied between one and three weeks. We are now of the opinion that when using doses designed to leave some viable cells, the best time to assess the damage is from seven to ten days after treatment Assessment later than this may be more difficult because surviving cells will have had time to produce fresh islets of growth—e g , case 4

We do not think that more conclusive evidence can be obtained from proceeding along these lines, and therefore we have planned a controlled trial using potentially curative doses to the whole tumour In this we also hope to ascertain the optimal pressure of oxygen though this is likely to vary for different tumours The work of Howard Flanders and Wright (1955) suggests that with irradiation to high dosage the addition of oxygen may bring an increased liability to bone necrosis owing to its normally poor oxygenation This difficulty is likely to be overcome when higher-energy irradiation becomes available because this is less absorbed by bone

Summary

A preliminary investigation was made in which eight patients with carcinomata were given radiotherapy while breathing oxygen at three atmospheres absolute

Satisfactory, though experimental, apparatus and technique are described

The results sufficiently suggest an increase in the radiosensitivity of tumours so treated as to warrant a more extensive trial

We express our gratitude to Sir Robert Davis without whose generosity in providing the pressure chamber this investigation would not have been possible; Dr L. H. Gray Dr O C A Scott Dr J A C Fleming Mr G H Bateman, Dr H J Taylor the surgeons and diving officers of H.M.S. *Vernon* and H M S *Reclaim* Dr A Glucksmann Dr F G Spear Dr P Bauwens, Dr G L Gryspeerdt Dr A. H Galley, Mr P Styles Mr P Tothill Mr A E Clark Mr H C Davies, the British Oxygen Company and the staff of Siebe Gorman Ltd for their assistance; Mr G Kent Harrison, who operated on the lung tumours Mr J Kodicek and the staff of the ear nose and throat department who performed the myringotomies Mr T W Brandon for the photographs and the staff of the radiotherapy department for treating these patients in their off-duty hours.

REFERENCES

Armstrong H W (1931) *Arch Otolaryng Chicago* 59 653
Bean J W (1945) *Physiol Rev* 25 1
Bert P (1878) La pression barométrique Paris
Churchill Davidson, I (1954) Personal communication
Donald K W (1947) *Brit med J* i 667 712
Gerschman R, Gilbert D L, Nye S W Dwyer P Fenn W O (1954) *Science* 119 623
Gray L H (1953) *Brit J Radiol* 26 609
— Conger A D, Ebert M Hornsey S Scott O C A (1953) *Ibid* p 638
Howard Flanders P Wright E A (1955) *Nature Lond* 175 428
Hultborn K A Forssberg A (1954) *Acta radiol* 42 475
Lambertsen C J Kough R, H Cooper D Y, Emmel G L, Loeschcke H H Schmidt C F (1953) *J appl Physiol* 5 471
Marks H P (1944) Unpublished
Paton W D M (1955) Personal communication
Sanger C Churchill Davidson, I Thomlinson R H (1955) In preparation.
Taylor H J (1954) Personal communication
Thomlinson R H Gray L H (1954) In British Empire Cancer Campaign annual report
— — (1955) In preparation
Thomson W A R (1935) *Brit med J* ii 208

THE pH AND BUFFERING POWER OF HUMAN BILE

N Crawford
F I M L T
CHIEF TECHNICIAN, SURGICAL RESEARCH LABORATORIES
B N Brooke
M D Birm , M Chir Camb , F R C S
READER IN SURGERY
UNIVERSITY OF BIRMINGHAM

Much time has been spent in investigating the relation of acid secreted in the stomach to ulceration in the duodenum, but little on determining the factors that may neutralise the acid The pH and buffering power of bile have been thoroughly investigated in animals, but scarcely at all in man and we describe here the results of such an investigation

Bile is commonly regarded as alkaline in reaction Okada (1916) stated that the pH varied between 7 7 and 8 6, but the specimens which he examined were pathological Most workers have obtained their material from biliary fistulæ, and loss of carbon dioxide may have affected their results The investigations of Barry and Levine (1924), Carnot and Gruzewska (1925), Stern (1926, 1928), and Reinhold and Ferguson (1929) reveal a pH range of 5 4 to 7 8 As regards buffering power, Jones (1930) found in dogs that hepatic bile was not as effective as pancreatic juice , Schultz Brauns (1927, 1929) showed, also in animals, that bile was weakly buffered when its acid content was low Neubauer (1923) investigated the buffering power of human bile , but since the indicators he used were phenol phthalein and methyl-red, the range investigated was pH 9 1 to 5 2—which is far removed from the pH of chyme as it enters the duodenum

Nature of Specimens

Bile was obtained from the gall-bladder at laparotomy 20 samples (classified as "normal") were taken from patients with no disease of the liver or biliary apparatus (laparotomy was done in 10 for duodenal ulcer, in 4 for gastric ulcer, in 2 for appendicectomy, and in 4 for diagnostic purposes) 10 samples of "abnormal" bile were obtained from patients with disease of the liver or ducts (7 with gall stones, and 3 with malignant dep in the liver)

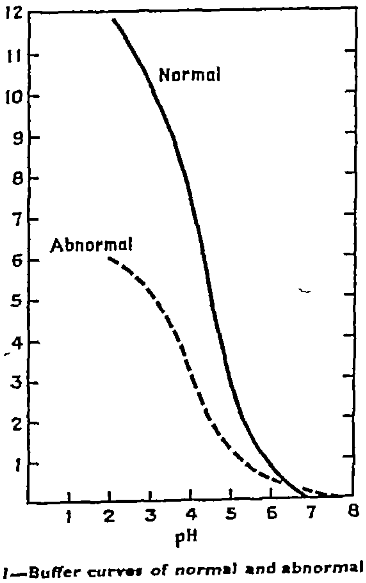


Fig 1—Buffer curves of normal and abnormal bile

7–10 ml of bile was aspirated through an 18-gauge into a sterile syringe lined with neutral paraffin. At first contents were discharged into a test tube under liquid which served as a seal against loss of carbon dioxide, this step was abandoned, and if storage was necessary analysis the bile was sealed in the syringe (a small of mercury being introduced for ease of subsequent and the whole placed in a refrigerator

Methods

The pH of each sample was determined by means direct reading meter, with glass electrode and calomel capable of recording to within 0 05 unit For buffering capacity, *titrations were made on 5 ml.* using 0 1*N* hydrochloric acid, since this reproduces the of gastric juice To determine the buffer value the quantity of acid added should, theoretically, be so as not to disturb the buffer acid/salt ratio , but a *approximation can be made by adding just sufficient to* a measurable change within the limit of accuracy meter For these titrations, therefore, 0 2 ml. of acid *added for each reading , titrations* ceased when the had been brought to pH 2 0 Thorough mixing was *at each addition of acid until a stable reading* was since surface acting agents such as bile salts prevent adjustment of potential Pilot experiments showed that bile suffered no alteration in buffer capacity, though the pH might alter within 0 5 of a unit, on exposure to periods of up *to 4 days Accordingly, no precautions* taken to avoid atmospheric contact during titration total solids in each sample were measured by drying oven at 110°C until a constant weight was reached

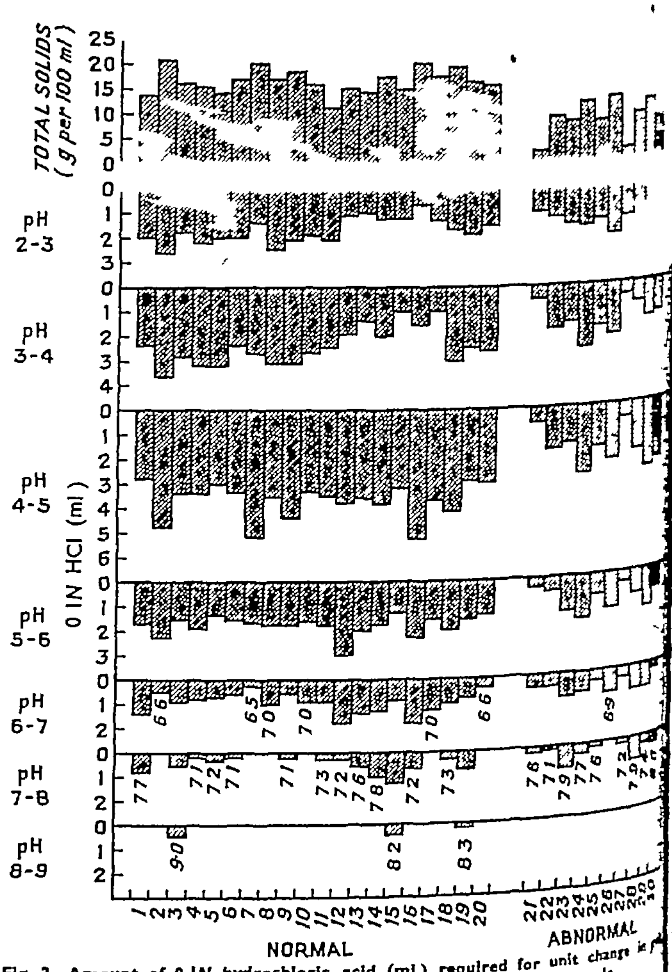


Fig 2—Amount of 0 1N hydrochloric acid (ml) required for unit change in pH of the sample
Figures under each column indicate original pH of the sample

Results

The pH of bile from 3 patients was acid (pH about
) in the 27 others it was either neutral or alkaline
e accompanying table) There was little difference
tween the 20 normal and the 10 abnormal samples
e ranges being 6 5–9·0 (mean 7 3) and 6 9–8 0 (mean 7 6)
pectively There was no apparent relationship between
e pH of each sample and its weight of total solids

Buffer curves were prepared by plotting pH readings
ainst the volumes of 0·1*N* hydrochloric acid added
g 1) For ease of comparison and better understanding
diagram has been constructed showing the amount of
d required for each unit change in pH (fig 2) In 28
mples it was found that the maximum buffering
pacity lay in the range pH 5–4 In no sample of normal
le was less than 2 9 ml 0 1*N* hydrochloric acid required
carry the pH from 5 to 4 (range 2 9–5 3 mean 3 7)
hereas none of the abnormal bile samples required
ore than 2 8 ml (range 0 7–2 8 mean 1 9) The total
lids were found to be related to the buffering capacity
d this was further reflected in the fact that the weight

Sample no	Initial pH	ml of 0 1*N* HCl needed to convert to pH 2·0	Total solids (g per 100 ml)
rmal			
1	7 9	11·0	13 7
2	6 8	13 8	21 0
3	9 0	11 4	15 7
4	7 1	11 6	15·6
5	7·2	10 5	14 0
6	7 1	10·0	16·8
7	6 5	11 4	20 0
8	7·0	12 0	16 6
9	7 1	12·0	18 2
10	7 0	10 4	19 1
11	7 3	11·0	11·4
12	7 2	11 0	15 3
13	7 6	8 9	11·4
14	7 8	11 1	17 2
15	8 2	9 2	14 8
16	7 2	12 2	21·0
17	7·0	9 0	17·3
18	7 3	12 1	19 2
19	8 2	10 5	16 9
20	6 6	9·0	15 8
an	7 3	11 0	16·6
nge	6 5–9 0	8 9–13 8	11 4–21 0
normal :			
21	7·0	3 4	3·8
22	7 1	6 0	9·2
23	7 9	8 2	8 0
24	7 7	10 0	12 1
25	6	6 4	8 5
26	8 0	9 9	12 8
27	7 2	3 6	4 7
28	7 0	6 0	9 4
29	7 1	8 2	11 7
30	8 0	7 7	10 7
an	7 6	7·0	9 1
nge	6 9–8 0	3 4–10 0	3 8–12 8

solids for normal bile samples was 11 0–21 0 g per
0 ml compared with 3 8–12 8 g per 100 ml for
normal bile The initial pH of a sample was no indica
n of the total buffering capacity to pH 2 0 for
ample sample 3 (see accompanying table) was alkaline
pH 9·0 but absorbed no more 0 1*N* hydrochloric
id than did sample 7 which was originally acid at
H 6·5

Summary

The pH of human bile obtained from the gall bladder is
ally neutral or alkaline but may occasionally be acid

The pH range of bile in patients without liver or biliary
ease does not differ from that in patients with such
ease but the buffering capacity is greater

Bile acts best as a buffer between pH 5 and pH 4.

The pH of bile does not vary with the proportion of
tal solids but the buffering capacity is apparently
ectly related to the weight of total solids In disease
the liver or biliary tract the total solids are decreased
d the buffering capacity is correspondingly diminished

References at foot of next column

THE DISPOSAL OF RADIOACTIVE POTASSIUM INJECTED INTRAVENOUSLY

D A K Black
M.D., B.Sc St And., F.R C.P
READER IN MEDICINE UNIVERSITY OF MANCHESTER

H E F Davies
M.D Lond., M.R C.P
MEDICAL RESEARCH COUNCIL CLINICAL RESEARCH FELLOW
ROYAL INFIRMARY MANCHESTER

E W Emery
B.Sc Ph.D Lond
LECTURER IN MEDICAL PHYSICS, UNIVERSITY OF MANCHESTER

By injecting tracer doses of ^{42}K intravenously, we can make manifest the transfer of potassium from the blood stream to the tissues

In any given capillary bed the amount of potassium exchanged will depend on the speed of perfusion, and on the speed of exchange of potassium across the capillary wall At one extreme the circulatory transit time of a potassium ion will be infinitely less than the time of exchange of K ions across the capillary wall which we may call exchange time , at the other extreme the exchange time will be infinitely less than the transit time.

The consequences of these two possibilities are predictable (fig 1) When the transit time is much shorter than the exchange time most of the entering K will leave in the venous blood there having been insufficient time for exchange the plasma ^{42}K level will fall only slowly and the organs will take up ^{42}K in proportion to their exchange rate for K On the other hand when the exchange time is much shorter than the transit time most of the entering K will go into the tissues the plasma ^{42}K level will fall very rapidly indeed and most of the injected ^{42}K will initially be found in those organs which have a high blood flow

This distribution of ^{42}K in proportion to blood flow will of course be transient for the same organs which rapidly take up ^{42}K when the plasma ^{42}K level is high will also discharge it when they are again perfused with K of low specific activity (S A)* and ultimately the various tissues contain ^{42}K in proportion to their content of chemical K

We summarise here the results of experiments which suggest that the initial uptake of ^{42}K by organs is a function of their blood flow rather than of their K content This suggests that for potassium, the rate of exchange in tissues is very high the exchange time being much less even than the short time taken for circulatory transit

Observations

Disappearance from Plasma

After rapid intravenous injection of a tracer dose (50–100 μC) of ^{42}K successive samples of arterial blood show a peak of activity about 50% of the dose per litre

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* The specific activity is the ratio of radioactive potassium (^{42}K) to total chemical potassium. In this work the amount of ^{42}K is expressed as a percentage of the dose—i e., the amount injected less the amount excreted—and chemical K is expressed as m eq Hence the S A is , dose/m.eq K.

MR CRAWFORD MR BROOKE REFERENCES

Barry W H Levine V E (1921) *J biol Chem.* 89 62
Carnot P., Gruzewska Z. (1925) *C R Soc. Biol Paris* 93 240
Jones K (1930) *Proc Soc exp Biol N Y* 28 567
Neubauer E. (1923) *Arch exp. Path Pharmak* 97 231
Okada S (1916) *J Physiol* 50 114
Reinhold J G Ferguson, L K (1929) *J exp Med* 49 681
Schultz Brauns O (1927) *Schweiz med Wschr* 8 [illegible]
— (1929) *Verh dtsch path Ges* 24 236
Stern R. (1926) *Arch exp Path Pharmak.* 112 1 9
— (1929) *Ibid* 131 2 1

of plasma at 20–30 seconds after the injection Thereafter the injected dose disappears very rapidly from the plasma at 2 minutes 5% of the dose per litre, or less, remains in the plasma, and at 5 minutes less than 1% These results in man are consistent with those obtained by Walker and Wilde (1952) in the rabbit, and by MacIntyre and Leonards (1955) in the dog

Renal Uptake of ^{42}K

The kidneys receive about 20% of the resting cardiac output, but their K content represents only 1–2% of the total body K Experiments on rabbits have shown that 2 minutes after the injection up to 10% of the injected dose can be demonstrated in each kidney (Emery et al 1955) The renal share of injected ^{42}K is clearly much more closely related to blood flow than to K content Kidneys taken out 30 minutes after the injection of ^{42}K contained only 2% of the dose, this disappearance of ^{42}K from the kidneys between 2 and 30 minutes could not be accounted for to any great extent by loss of ^{42}K in the urine, because this was only 1% or less of the injected dose It seemed likely that most of the ^{42}K was returned to the renal venous plasma, but we could not examine this point adequately in rabbits Two experiments in volunteers have shown that during the first half-hour after injection the K of renal venous plasma is of a specific activity higher than that of systemic plasma, and comparable to that of urine—i e, 2–5 times the systemic S A

The unique disproportion between blood-flow and K content in the kidneys makes the dependence of renal ^{42}K uptake on blood flow rather easy to demonstrate, our evidence on other tissues is less conclusive but in no way conflicts with the view that blood-flow is more important than K content in deciding the *early* uptake of ^{42}K

Uptake by Gut and Liver

After oral administration of ^{42}K the S A in the plasma increases slowly, but after 20 minutes it is maintained at a higher level than after intravenous injection (fig 2) Some of this "delay" must be due to the time needed for intestinal absorption, but we believe that the subsequent maintenance of plasma S A is largely due to the discharge of a pool of K of high S A in the gut and liver It is known that 2 minutes after intravenous injection of ^{42}K in the rabbit about 35% of the injected dose can be found in the gut and liver (Walker and Wilde 1952) One minute after intrasplenic injection of small amounts of ^{42}K in the rat more than 50% of the injected dose is commonly found in the liver (G A Lumb, R F Mahler, and S W Stanbury, personal communication), whereas the amount found in the liver after intravenous injection is about 5% (Ginsburg and Wilde 1954) These various observations suggest that gut and liver can take up a high proportion of the K in the blood supplied to them, exchanging cellular K for it

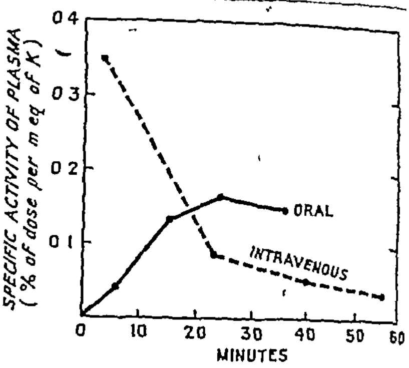

Fig 2—Time-course of specific activity of plasma-K after intravenous and oral administration of ^{42}K.

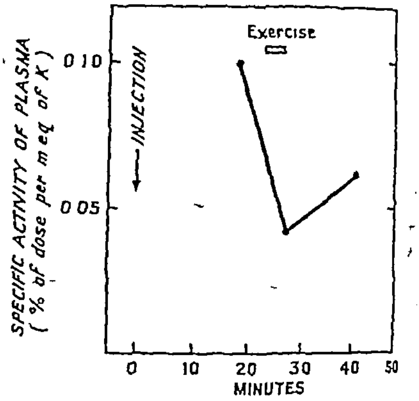

Fig 3—Depression of specific activity of plasma-K by exercise. (Normally, plasma S.A. is steadily falling at this time—cf fig 2.)

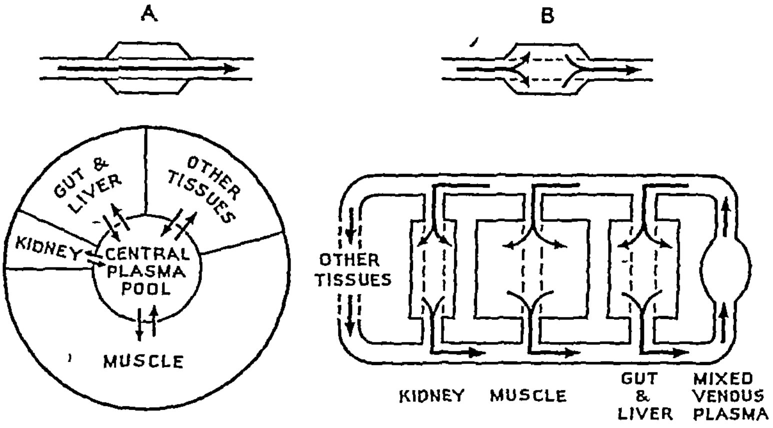

Fig 1—Mechanism of distribution of K among tissues Two limiting cases are shown:

(A) Only a small fraction of plasma K is exchanged during each transit, with the result that the K leaving an organ is essentially that which entered it In these circumstances individual tissues compete for intravenously injected ^{42}K and will take it up in proportion to their exchange rate The activity in the central plasma pool will fall steadily until plasma and tissues are in equilibrium

(B) Almost all the plasma K is exchanged in each transit, with the result that the K leaving the tissue is derived from tissue K rather than from arterial K Intravenously injected ^{42}K will be very quickly cleared from plasma and deposited in the various tissues according to their relative blood flow During subsequent redistribution the specific activity of mixed venous plasma may actually increase, if the circulation is increased through tissues containing K of high specific activity

Uptake by Muscle

Although more than half the body K is in muscle, the blood flow in resting muscle is only about 3 ml per minute per 100 g, in contrast to 270 ml for kidney, and 70 ml for liver (Edholm 1953) In so far as early uptake of ^{42}K is determined by blood flow, muscle will come off very badly relative to its K content, and the K in muscle soon after intravenous injection will be of low S A If blood flow through muscle is then increased by exercise, and if venous effluent from a tissue is mainly derived from tissue K, generalised exercise should produce a "dip" in the curve of plasma S A Such a "dip," induced by weight lifting, is shown in fig 3

It is impossible in man to determine the S A of K in various tissues at intervals after injection of ^{42}K Our own data on rabbits are very limited but Ginsburg and Wilde (1954) have published extensive observations of this type on rats Fig 4 is constructed from their results and shows rather clearly how the initial distribution of ^{42}K depends very largely on blood flow, whereas subsequently redistribution occurs, with an approach to the uniform distribution of ^{42}K which permits the measurement of exchangeable potassium

Conclusions

These findings strongly suggest that the exchange of K between plasma and tissues takes place so rapidly that the K of arterial plasma is largely, if not wholly superseded in venous plasma by K derived from the tissue during transit If this is correct certain consequences follow A tracer dose of ^{42}K given intravenously is almost at once distributed among the organs of the body in proportion to their relative blood supply This initial disposal of injected ^{42}K is followed without pause by a redistribution of ^{42}K whose end result is that the various organs contain ^{42}K in proportion to their potassium content The speed with which the S.A in each organ approaches the final equilibrium value (or more strictly, the S.A in current arterial plasma) will be directly proportional to the blood flow through it and inversely proportional to its K content Since the K in the venous drainage from a tissue is derived from the K content of the tissue the S.A of the mixed venous blood can be raised (or lowered) by altering the circulation so that organs which at the time contain K of high (or low) S.A make a greater contribution to the total venous flow

Even if this theoretically derived pattern of K distribution is only partially correct (and some organs, such as brain are exceptional in their behaviour) our actual results show that tissue and plasma S.A can be greatly influenced by blood flow This makes it unlikely that observations on the amount of ^{42}K in plasma or in individual organs can give any definite information on alterations in the rate of exchange of K across the cell membrane during the phase of initial disposal and subsequent redistribution This type of approach is therefore unlikely to yield useful conclusions on the state of the potassium household

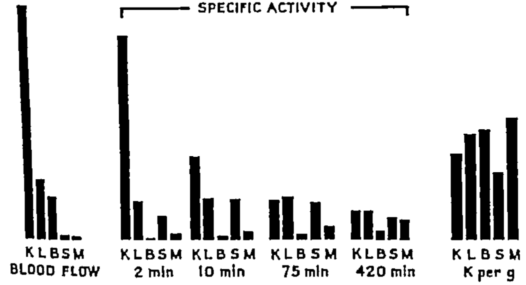

Fig 4—Comparison of time-course of intravenously injected ^{42}K with relative blood flow and relative tissue-K content in kidney (K) liver+gut (L) brain (B) skin (S) and muscle (M) The early distribution of ^{42}K resembles relative blood-flow the later distribution tends towards relative K content; brain tissue is anomalous in its slow rate of uptake of ^{42}K relative to its blood-flow Constructed from results of Ginsburg and Wilde (1954) with the estimates of Edholm (1953) of relative blood-flow

It seems likely that this pattern of distribution is characteristic not of potassium as such but of any substance which leaves the blood stream rapidly in relation to circulatory transit time. In hind limb perfusion experiments Pappenheimer et al (1951) demonstrated a disappearance rate from plasma of this order of rapidity for substances as diverse as chloride deuterium oxide inulin and glucose There are of course substances such as plasma albumin which leave the circulation only slowly and Elgee et al (1954) have shown that the early uptake of ^{131}I tagged albumin is very much less in both liver and kidney than we have described for ^{42}K These two types of behaviour may correspond in a general way to cases A and B in fig 1 A high immediate uptake of a tracer tagged substance by organs with a high blood flow—e g liver and kidney—may be taken as presumptive evidence of rapid transcapillary exchange of that substance

REFERENCES

Edholm O G (1953) Lectures on the Scientific Basis of Medicine London vol 1 p 9
Elgee N J., Williams R. H Lee N D (1954) *J clin Invest* 33 1[illegible]
Emery E. W Holmes R. Davies H E F Black D A K (1955) *Clin Sci* (in the press)
Ginsburg J M., Wilde W S (1954) *Amer J Physiol* 179 63
MacIntyre W J Leonards, J R (1955) *Circulation Res* 3 11
Pappenheimer J R. Renkin E. M Borrero L M (1951) *Amer J Physiol* 167 13
Walker W G Wilde W S (1952) *Ibid* 170 401

PRESSURE AND DURATION OF INSPIRATION DURING ARTIFICIAL RESPIRATION BY INTERMITTENT POSITIVE PRESSURE

J M K. SPALDING
M.A D M Oxfd M R C P
ASSISTANT DEPARTMENT OF NEUROLOGY RADCLIFFE INFIRMARY OXFORD

ARTIFICIAL respiration by intermittent positive pressure through a tracheostome was introduced in Denmark for the treatment of poliomyelitis (Lassen 1953) and has since been used for that disease for polyneuritis (Crampton Smith et al 1954 Macrae et al 1954 Harries and Lawes 1955), and for severe tetanus treated with relaxants (Bjorneboe et al 1953 Shackleton 1954 Honey et al 1954 Lassen et al 1954)

There is plenty of evidence to indicate that such patients can be kept in reasonably good condition by intermittent positive pressure respiration for many months An acute respiration unit however has to deal with patients in a critical state either from pulmonary complications or from circulatory failure and if such patients are to be saved the factors affecting ventilation provided by intermittent positive pressure must be investigated and considered in connection with the effect of such pressure on the circulation To ascertain the factors at work it is necessary to analyse the effects of changes of inspiratory pressure duration of inspiration and respiratory rate

Method

Measurements have been taken on adults with severe respiratory paralysis who were receiving artificial respiration by intermittent positive pressure through a tracheostome Patients who are not paralysed are not suitable for this type of investigation because muscle tone varies and tends to keep the respiratory minute volume constant (Yandell Henderson 1938) A Stott expiratory valve (Crampton Smith et al 1954) was used and tidal air was measured either by collecting expired air in a spirometer or by passing it through a dry gasmeter * The tidal air recorded is the mean of ten or more respirations Pressure was recorded close to the external end of the tracheal tube and the duration of inspiration was determined by measurement from the pressure records examples of which are shown in fig 5

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* Type C D 1 Meter (Parkinson & Cowan Industrial Products London)

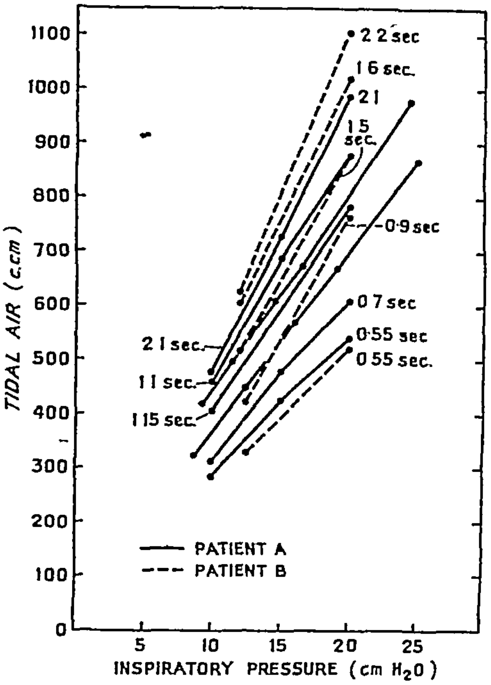

Fig 1—Relationship of tidal air to inspiratory pressure in patients with healthy lungs Duration of inspiration is given in seconds. The pressure record obtained was similar to curves a and b in fig 5

Influence of Inspiratory Pressure on Tidal Air

Fig 1 indicates the changes in tidal-air that result from alterations in the inspiratory pressure The measurements were taken from two patients Patient A had a vital capacity of only 400 c cm, and patient B had complete paralysis of primary and secondary respiratory muscles The lungs of both were healthy Pressures from 9 to 25 cm water, and tidal air from 275 to 1100 c cm, were investigated Fig 1 shows that the tidal air increased in almost direct proportion to inspiratory pressure Fig 2 shows curves taken from patient C, whose bronchial tree contained much secretion When curve *a* was obtained, air entry was generally poor, especially on the left side, and altogether absent over the left lower lobe The curve *c* shows that an increase of pressure of 5 cm water increased the tidal air by only 15 c cm instead of the 100 c cm that would be expected from fig 1 After vibration and percussion of the chest, a gobbet of secretion was aspirated, and air entry on the left side of the chest was considerably improved, though not normal Curve *b* was then obtained about 30 minutes after curve *a*. The situation was improved in that at an inspiratory pressure of 17 5 cm water 120 c cm was added to the tidal air, and at lower pressures the direct relationship between pressure and tidal air was re established At higher pressure, however, the well marked flattening of the curve returned Curve *c* taken a few weeks later, when the chest was clinically and radiologically normal, shows that the pressure/tidal-air relationship was practically normal

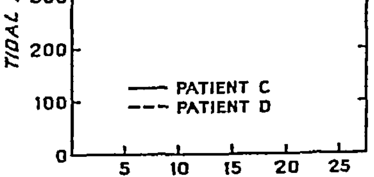

Fig 2—Relationship of tidal air to inspiratory pressure in two patients with abnormal lungs *a*, from patient C with major bronchial obstruction, *b*, after partial clearance *c*, after complete clearance of obstruction *d* from patient D with tetanus when partially curarised, *e*, when fully curarised Gravity operated pump, giving pressure records of type fig 5c was used in plotting curves

Curves *d* and *e* were taken from a patient with severe tetanus treated with paralysing doses of curare (Honey et al 1954) When curve *d* was obtained, the patient was minimally curarised, and owing to muscular rigidity the tidal air was small and was not increased by a rise in pressure Tubocurarine 15 mg was given intravenously, and curve *e* was obtained shortly after The normal relationship of pressure to tidal air was re-established by relaxing the muscles

Conclusion — In the paralysed patient with healthy lungs the tidal air is proportional to the inspiratory pressure within the limits of 275–1100 c cm of tidal air and a peak pressure of 9–25 cm water If, however, there is major bronchial obstruction or much muscular rigidity, as in tetanus, an increase in pressure may produce virtually no increase in tidal air

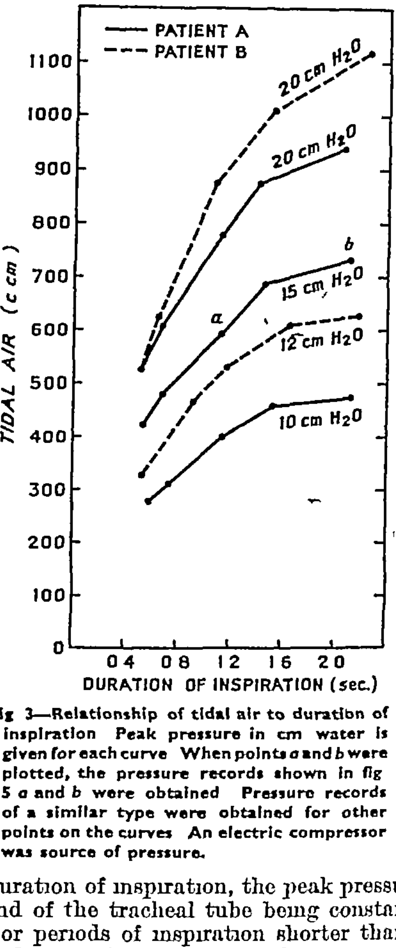

Fig 3—Relationship of tidal air to duration of inspiration Peak pressure in cm water is given for each curve When points *a* and *b* were plotted, the pressure records shown in fig 5 *a* and *b* were obtained Pressure records of a similar type were obtained for other points on the curves An electric compressor was source of pressure.

Influence of Duration of Inspiration on Tidal Air

Fig 3 shows the effect on tidal air of varying the duration of inspiration, the peak pressure at the external end of the tracheal tube being constant for each curve For periods of inspiration shorter than 1 5 sec. there is a distinct decrease in tidal air as inspiration becomes shorter, but the reduction in tidal air is by no means directly proportional to the shortening of inspiration When inspiration exceeds 1 5 sec in duration, the increase in tidal air is only slight The flattening of the gradient in the curves in fig 3 when inspiration is prolonged indicates that, though air continues to enter the patient's lungs even after inspiration has continued for 1 5 sec., its rate of flow is much slower at the end than at the beginning For instance, at a peak pressure of 15 cm water, in the first 0 7 sec 480 c cm of air enters the lungs, in the next 0 7 sec only 190 c cm does so, and in a further 0 7 sec only 55 c cm enters

RELATION OF TOTAL TO EFFECTIVE MINUTE VOLUME

Rate per min	Tidal air (c cm)		Minute volume (c cm.)	
	Total	Effective	Total	Effective
15	600	500	9000	7 5
25	400	300	10,000	7 5

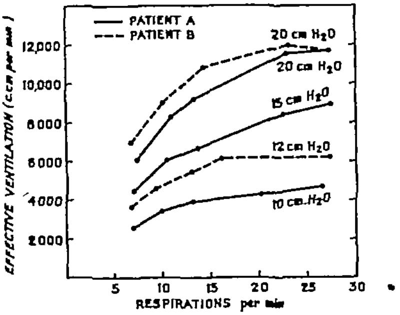

Fig 4—Effective minute volume at different respiratory rates in patients with healthy lungs. Peak inspiratory pressure for each curve is given in cm. of water.

Conclusion.—Within the range of duration of inspiration 0·6–2·2 sec. although the amount of tidal air decreases as inspiration is shortened the relationship is not directly proportional. Inspiration longer than 1·5 sec. provides little useful increase in tidal air.

Influence of Respiratory Rate on Effective Ventilation

Where efficiency of ventilation is concerned it is not total tidal air but effective tidal air (total tidal air minus dead space) that is important. In the presence of a tracheostome the dead space is decreased by by passing the larynx and upper respiratory tract and by introducing a tube into almost the whole length of the trachea. This is partially offset by the volume of the tubing between the patient and the expiratory valve, which is about 15 c cm. For the present purpose the dead space in a patient receiving artificial respiration by intermittent positive pressure is taken to be 100 c.cm. In comparing ventilation at different rates therefore, 100 c.cm. per breath must be deducted from the actual minute volume to give the effective volume. An example is given in the accompanying table which shows that to provide an effective minute volume of 7500 c cm. a total minute volume of 9000 c.cm is required at a rate of 15 respirations per minute and of 10 000 c.cm. at 25 respirations per minute. An extra 1000 c cm. per minute has therefore to be provided at the faster rate to achieve the same ventilation.

There is a further factor to be considered when the respiratory rate is raised—namely that an increase in the respiratory rate reduces the duration of inspiration proportionately. Fig 4 shows the relationship of effective minute volume (i e of actual ventilation) to actual respiratory rate at various pressures making allowance for the shortening of inspiration as the respiratory rate rises. In deriving fig 4 from fig 3 the duration of inspiration has been taken as a quarter of the respiratory cycle. The shape of the curves, however, is not materially altered if another proportion is chosen though they are shifted to the right or the left. At no point does an increase in respiratory rate produce a proportionate increase in ventilation and at rates above 16–20 per minute a considerable rise in rate is necessary to produce an appreciable rise in effective minute volume. Thus by doubling the respiratory rate from 13 to 26 per minute the effective minute volume is increased on the average by little more than 20%.

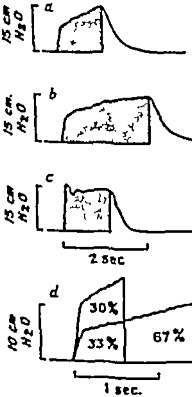

Fig. 5—Pressure at external end of tracheal tube with inspiratory period stippled. Records of type a and b were used in figs. 1, 3 and 4; and of type c in fig 2; d shows two pressure records providing the same amount of tidal air.

Conclusion.—Increase in respiratory rate is a relatively unsatisfactory way of increasing ventilation. Ventilation of the dead space and shortening of the inspiratory period make the increase in actual ventilation slight. This is more particularly the case when the respiratory rate exceeds 16–20 per minute.

Discussion

The observations given above have implications both for the management of patients and for the design of apparatus. They indicate that for the patient without pulmonary complications an increase in ventilation is most readily obtained by increasing the inspiratory pressure. Where complications are present, it may be necessary to increase the respiratory rate, but a considerable increase in rate is required to increase the actual ventilation appreciably. In all cases therefore, it is essential to measure the tidal air directly when the setting of the apparatus is changed and not to rely on deductions from pressure readings. Moreover, in assessing ventilation the effective not the gross minute volume must be considered.

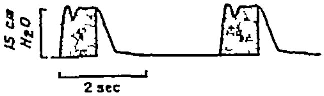

Fig. 6—Pressure record shewing how small the proportion of inspiration can be to the whole respiratory cycle.

One of the dangers of artificial respiration either in a tank respirator or by intermittent positive pressure lies in the strain it places on the circulation by impeding blood flow into the right side of the heart (Werkö 1947, Cournand et al. 1948, Motley et al 1948, Hubay et al 1954). Compensatory mechanisms normally enable a satisfactory cardiac output to be maintained; but if the circulatory mechanisms have been damaged, satisfactory compensation may not be possible. Circulatory mechanisms may be damaged in poliomyelitis by involvement of the circulatory centre and in polyneuritis (Clarke et al 1954). A *similar state of affairs* has been observed in a patient with severe head injury whose respiration had to be maintained by intermittent positive pressure and whose blood pressure became unrecordable during inspiration, recovering to 90/50 mm. Hg during expiration. It is therefore necessary when treating acute cases of any type to allow the circulation every facility for compensation particularly by keeping the inspiratory period as short as possible and so providing the maximum period during which intrathoracic pressure is atmospheric.

Though the *most important factor in* easing the strain on the circulation is probably that inspiration should form a small proportion of the respiratory cycle the circulatory changes have also been correlated with the mean pressure in the face mask or in the type of patient considered here at the external end of the tracheal tube (Werkö 1947, Cournand et al 1948, Motley et al 1948). From fig 3 it can be seen that for example, a tidal air of 400 c cm. could be provided for patient A by an inspiration lasting either 1·5 sec. at a pressure of 10 cm water or 0 64 sec at a pressure of 15 cm water The mean pressure with the shorter inspiration is 30% less than with the longer (fig 5) though the amount of tidal air is the same It is therefore evident that, for a severely ill patient, a short period of inspiration can be used with benefit to the circulation without imperilling the ventilation If inspiration occupies a quarter of the respiratory cycle, there is an inspiratory period of 1 25 sec at 12 respirations per minute, and 1 0 sec at 15 respirations per minute A pressure curve of this type (fig 6) is also suitable for long term treatment and has been used routinely on patient A for ten weeks

Summary

Factors have been investigated which influence the artificial ventilation of paralysed patients by intermittent positive pressure

When the patient's lungs are healthy, the amount of tidal air is almost directly proportional to the inspiratory pressure When, however, there is major bronchial obstruction or (as in tetanus) rigidity of the respiratory muscles, an increase in pressure may produce little or no increase in tidal air

A large proportion of tidal air enters during the early part of inspiration, with the result that adequate tidal air may be obtainable by an inspiratory phase lasting only 0 6 sec Little is gained by prolonging it beyond 1 5 sec, and to do so embarrasses the circulation without providing any compensatory advantage. For the benefit of the circulation in acutely ill patients, inspiration may be reduced to a quarter of the respiratory cycle without prejudice to ventilation

This work has been done in the respiration unit at the Radcliffe Infirmary directed by Dr W Ritchie Russell I wish to thank him and Dr Crampton Smith for much assistance and advice

REFERENCES

Bjørneboe M, Ibsen, B, Johnsen, S (1953) *Ugeskr Laeg* **115**, 1535
Clarke E, Bayliss, R I S, Cooper, R (1954) *Brit med J* ii, 1504
Cournand, A, Motley, H L Werkö L Richards D W jun (1948) *Amer J Physiol* **152**, 162
Harries J R, Lawes W E (1955) *Brit med J* i 448
Henderson Y (1938) Adventures in Respiration London
Honey G E, Dwyer B E Smith, A C, Spalding J M K (1954) *Brit med J* ii, 442
Hubay C A, Waltz, R C Brecker G A, Praglin J Hingson, R A (1954) *Anesthesiology*, **15** 445
Lassen, H C A (1953) *Lancet* i, 37
— Bjørneboe M, Ibsen, B, Neukirch F (1954) *Ibid* ii, 1040
Macrae J, McKendrick G D W, Sefton E M, Walley, R. V (1954) *Ibid*, p 21
Motley, H L, Cournand A, Werkö L Dresdale D T, Himmelstein A, Richards, D W (1948) *J Amer med Ass* **137**, 370
Shackleton P (1954) *Lancet*, ii, 155
Smith, A C Spalding, J M K Russell, W R (1954) *Ibid*, i, 939
Werkö, L (1947) *Acta med scand* suppl no 193

TETRACYCLINE

R L McCorry
M B Belf M R C P I
REGISTRAR IN CLINICAL PATHOLOGY

J A Weaver
M D Belf, M R C P
REGISTRAR IN MEDICINE

From the Royal Victoria Hospital, Belfast, and the Department of Medicine, Queen's University of Belfast

Tetracycline ('Achromycin') is a recently developed antibiotic whose structure and antimicrobial spectrum are very similar to those of chlortetracycline ('Aureomycin') and oxytetracycline ('Terramycin') All three substances have the same chemical nucleus, chlortetracycline differs from tetracycline by the addition of a chlorine atom, and oxytetracycline by the addition of a hydroxyl group, thus tetracycline is the basic structure of the series

Clinical reports by Finland et al (1954) and Wood et al (1954) suggest that tetracycline is as effective therapeutically as the other two antibiotics and in fact may possess certain advantages These include a lower incidence of toxic side effects, and rapid achievement and maintenance of therapeutically effective levels in the serum

To assess its clinical usefulness we have studied the effects of oral administration on 87 patients admitted to the wards of the Royal Victoria Hospital, Belfast Particular attention was paid to the incidence of side effects and to the serum levels achieved by various oral doses The sensitivity of pathogenic organisms, isolated from patients in the hospital, to tetracycline was also studied

Antibacterial Activity

Methods and Materials

Single colonies of the strains required were picked off the routine plates, grown in nutrient broth, and stored until it was convenient to test them The minimal inhibitory concentration for each strain was estimated in the following manner

Tetracycline was incorporated in nutrient agar plates in concentrations ranging from 0 125 µg per ml to 10 µg per ml. The strains to be tested were transferred from 18 hour broth cultures to the plates In each series a plate which contained no tetracycline was included, and on each plate three strains of known sensitivity were streaked *Bacillus cereus* NCTC 8035 sensitive to less than 0 125 µg per ml of tetracycline, *B cereus* NCTC 7464 resistant to more than 2 5 µg per ml. but sensitive to less than 5 0 µg per ml, and a strain of *Pseudomonas pyocyanea* resistant to more than 10 µg per ml

TABLE I—MINIMAL INHIBITORY CONCENTRATION OF TETRACYCLINE FOR 71 STRAINS OF COMMON PATHOGENS

Organism	No of strains	Minimal inhibitory concentration (µg per ml)								
		0 125	0 25	0 5	0 75	1 0	1 5	2 5	5 0	Resistant to >10
B cereus 8035	1	1								
B cereus 7464	1								1	
Ps pyocyanea	3									3
Staph aureus	16	12								4
Strep pneumoniæ	2		2							
Strep hæmolyticus	5	1	4							
Strep viridans	11		2	5	2			1	1	
Strep fæcalis	8		3		3					2
Esch coli	19				12	4	1			2
Bact aerogenes	2					2				
Friedländer's bacillus	3				1	2				

Numerals indicate number of strains inhibited by that concentration and not by any lower concentration

No difficulty was experienced in assessing results, organisms either grew or did not grow

Results

It will be seen from table I that tetracycline is effective against both gram-positive and gram-negative organisms. Gram-negative organisms tended to have higher minimal inhibitory concentrations than did gram positive organisms Organisms may be divided into four main groups

(1) *Those inhibited by 0 25 µg per ml or less*—Among these are the sensitive strains of staphylococci, the pneumococci, the β hæmolytic streptococci, some of the α hæmolytic streptococci, and some enterococci All these organisms are gram positive

(2) *Those inhibited by concentrations greater than 0 25 µg but less than 0 75 µg per ml*—In this group are most of the strains of *Escherichia coli*, one strain of Friedländer's bacillus, many of the α hæmolytic streptococci, and some strains of *Streptococcus fæcalis*

(3) *Those inhibited by concentrations between 0 75 µg per ml and 1 5 µg per ml*—In this group are the strains of *Bacterium aerogenes*, two strains of Friedländer's bacillus, and several strains of *Esch coli*

(4) *Those which are resistant to more than 10 µg of tetracycline per ml*—In this group are found all the strains of *Ps pyocyanea* and some strains of *Staphylococcus pyogenes*, *Strep fæcalis*, and

Esch. coli Because the strains were drawn from hospital specimens it is impossible to be certain if these were naturally resistant strains or had acquired resistance The latter is probable in some cases. Several strains fell outside the groups but they were not considered to be important

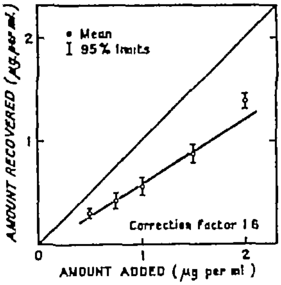

Fig 1—Four-point punch-plate assay of tetracycline: recovery curve Each point is the mean of 10 estimates; 95% confidence limits (2 S.E.M) are marked.

Blood levels

Method

The method was an adaptation of that used by Nelson et al (1954) in the assay of blood penicillin levels The pH of the media was reduced to 6·5 and the indicator organism was *B cereus* (NCTC 8035 Lederle no 5 strain) This method as used in this investigation has certain limitations recovery levels are about 60% between 0·5 µg per ml and 2·0 µg per ml with aqueous standards and accuracy is poor below 0·5 and above 2·0 µg per ml when the standards used are limited to 1·0 and 2·0 µg per ml as in this investigation This method is however simple and *economical of time and material*, and allowed triplicate plates to be used for each estimation Fig 1 shows the graph of recovery levels. Each point represents the mean of ten estimates the 95% confidence limits for each mean are marked

Results

On a dosage of 0·25 g 6 hourly blood tetracycline levels of about 0·75 µg per ml were attained on an average at the end of 16–18 hours Some patients were slow to produce therapeutic blood levels an experience shared by Putnam et al (1953) Because of this and because Transatlantic workers had noted a higher incidence of side-effects with larger doses it was decided to try the effect of a loading dose combined with the 1·0 g daily dosage Accordingly 6 patients were given 1·0 g at the start of treatment and maintained with 0·25 g 6 hourly This mode of treatment produced good blood levels (fig 2) The average level had risen to more than 1·0 µg per ml at the end of 2 hours and at the end of 4 hours the mean blood level was 1·4 µg per ml., with all the levels in the range 0·8–2·2 µg per ml At the end of 24 hours the mean blood level was about 3·0 µg per ml , and no level was below 1·5 µg per ml

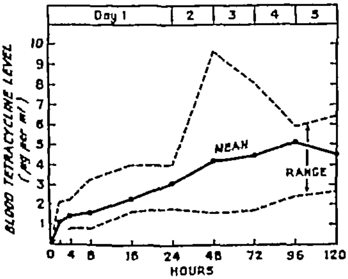

Fig 2—Blood-tetracycline levels obtained in 6 cases with an initial dose of 1 g followed by 0·25 g six-hourly

Clinical Results

Most of the 87 patients in this series were treated for acute infections of the respiratory system The clinical response (table II) was assessed on the duration of pyrexia *subjective improvement, and objective physical and* radiological findings

In *pneumococcal lobar pneumonia* the results obtained were good and in every respect equal to those following the use of chlortetracycline and oxytetracycline

In *acute bronchopneumonia* the results were variable and difficult to assess owing to many other complicating disease processes being present—e g cardiac failure Drug treatment was of necessity started before sputum results were available The organisms isolated from the sputum and considered to be pathogenic were mainly hæmolytic streptococci pneumococci staphylococci, and *Hæmophilus influenzæ* Three patients in this group had on admission been started on penicillin therapy without response and culture of the sputum showed the predominant organism to be Friedländer's bacillus in 2 of these cases and *H influenzæ* in the 3rd When the treatment was later changed to tetracycline in these cases the improvement was dramatic Generally the results in this group were again comparable to those observed with the two analogues

Of the 30 cases of pneumonia of all types it was considered that in 10 cases the response had been less than expected Of these 10 patients 4 had diarrhœa and this side effect exerted an unfavourable influence on the course of the primary illness The remaining 6 patients had other complicating features: 4 had congestive cardiac failure and 2 of these died and 2 had sinusitis.

TABLE II—RESULTS OF TREATMENT IN 87 PATIENTS

Diagnosis	No of cases	Good response	Toxic effect and complication	Poor or no response	Toxic effect and complication
Lobar pneumonia	12	11	0	1	1 diarrhœa
Broncho pneumonia	27	18	0	9	3 diarrhœa 2 sinusitis 4 congestive cardiac failure (2 died)
Chronic bronchitis	17	13	0	4	3 emphysema 1 asthma
Bronchiectasis	8	6	0	2	1 diarrhœa 1 abscess formation
Urinary infection	10	8	1 diarrhœa	2	2 proteus infection
Miscellaneous group	13	11	1 diarrhœa	2	0

Streptococcal pharyngitis (4) carbuncle (3) appendix abscess (2) parotitis (1) epididymitis (1) cholecystitis (1) and glandular fever (1)

Acute exacerbations of chronic bronchopulmonary suppuration formed the next largest group which was composed of chronic bronchitic patients who had developed frankly purulent sputum without pyrexia The *sputum contained mixed cultures of pathogens* mainly similar to those found in the patients with acute bronchopneumonia The results in this group judged by the diminution in amount and purulence of the sputum and by the subjective improvement were surprisingly good and usually better than those following inhalational therapy with either streptomycin or penicillin 4 patients in this series showed no improvement during treatment 1 had recurrent asthmatic attacks and the 3 others had associated advanced emphysematous changes The presence or absence of emphysema and asthma seems to be more important than the nature of the infecting organism in determining the response of a chronic bronchitic to antibiotics Helm et al (1954) also emphasise the importance of deciding whether the asthma is infective or non infective before treating it with antibiotics.

TABLE III—UNTOWARD EFFECTS OF TETRACYCLINE

Daily dose (g)	No of cases	Untoward effects
1	60	5 diarrhœa 12 nausea, 2 skin rash
2	11	2 diarrhœa 1 nausea
Initial loading dose 1, followed by 250 mg 6 hourly	16	1 diarrhœa

Bronchiectasis —There was a temporary improvement with lessening of the amount of sputum in 6 of the 8 patients

Miscellaneous Infections —In this group the number treated was small, but the favourable outcome in the majority of cases compares again with the results obtained with the two analogues In the urinary infections with *Esch coli* the response was particularly good

Side-effects

The side effects so far recorded with the tetracycline group have been mainly gastro-intestinal—e g , flatulence, nausea and vomiting, diarrhœa, and pruritus ani Skin reactions of an allergic type have also been noted (Putnam et al 1953) The pathogenesis of these bowel upsets is not clear , it is generally thought that the upper-intestinal symptoms of nausea and vomiting are related to the chemical structure of tetracycline, and that the diarrhœa is associated with alterations in the intestinal flora secondary to the antimicrobial effect Furthermore, the nausea and vomiting do not necessarily occur in the patients who experience diarrhœa and pruritus ani

Table III shows the incidence of the side-effects in the 87 patients on tetracycline therapy In table IV we have compared the occurrence of the gastro intestinal side-effects in the tetracycline group with comparable groups of patients receiving chlortetracycline and oxytetracycline in equivalent dosage, and in the hospital at the same time The incidence of diarrhœa was roughly similar in all three groups, being highest with oxytetracycline In the 8 cases of diarrhœa in the tetracycline series a careful search was made of the stools for pathogenic organisms Despite the use of selective media, the fæces in all the cases produced a pure growth of *Proteus vulgaris*, but in many other patients who did not experience diarrhœa the predominant organism in the fæces from the fourth day onwards was *P vulgaris*

TABLE IV—COMPARISON OF GASTRO INTESTINAL SIDE EFFECTS OF TETRACYCLINE, CHLORTETRACYCLINE, AND OXYTETRACYCLINE (1 G DAILY)

—	Tetracycline	Chlortetracycline	Oxytetracycline
No of cases	60	60	60
Diarrhœa	5 (8 %)	4 (7 %)	7 (12 %)
Nausea	2 (3 %)	10 (17 %)	7 (12 %)

The incidence of nausea is also shown in tables III and IV , when tetracycline and chlortetracycline were compared in a $2 \times 2\chi^2$ table, it was seen that tetracycline gave rise to significantly less nausea ($0\ 05 > P > 0\ 02$) The numbers were insufficient to carry out this analysis between tetracycline and oxytetracycline, but it will be seen that there is again a lower incidence in the tetracycline group The much greater freedom from gastric upset in the tetracycline group was clearly illustrated in 1 patient who was treated with oxytetracycline, chlortetracycline, and tetracycline successively

A stitcher, aged 20, underwent valvotomy for mitral stenosis in May, 1954 Postoperative pyrexia developed, and blood cultures showed a *Salmonella london* bacteræmia Treatment was begun with oxytetracycline 500 mg 6 hourly After each dose of the tablets nausea and vomiting came on A change to chlortetracycline did not relieve the gastro-intestinal symptoms , but, when tetracycline was substituted, the nausea and vomiting ceased, and therapy was continued with tetracycline for a month

One of the controls had a duodenal ulcer On therapy with oxytetracycline 1 g daily he experienced, after each dose, considerable epigastric burning discomfort which he considered to be exactly like his previous symptoms during an exacerbation of his peptic-ulcer state This suggests that the upper intestinal effects are due to direct irritation of the mucosal surfaces

Discussion

Clinical Results

The clinical outcome in the group of infections treated with tetracycline was very similar to that following the use of chlortetracycline and oxytetracycline and confirms the suggested equivalent therapeutic activity within this group The fact that there is less chance of encountering a resistant organism with the tetracyclines than with penicillin has encouraged some workers to recommend the universal use of the tetracyclines in these acute chest conditions This advantage is somewhat offset by the quicker action and lesser side-effects of penicillin in the infections with sensitive organisms, and for that reason we feel that penicillin should still remain the drug of choice in the initial treatment of pneumonia, and that tetracycline should be reserved for cases which do not respond to penicillin, or where the causal agent has been shown to be penicillin-resistant

In short-term treatment of acute exacerbations of chronic bronchitis tetracycline was extremely effective, and with judicious use the incidence of side-effects is not such as to preclude its use in this type of case. What effect the treatment of acute exacerbations will have on the long term outlook in chronic bronchitis is problematical, but such treatment seems worth trying in view of the eventual complications of this disease The only real barrier appears to be the cost of treatment. but this should probably become less with increasing production, as has happened with penicillin

Side effects

There has been considerable variation (3–30%) in the reported incidence of side effects with the tetracycline analogues, and this has rendered the comparison of results very difficult This variation has been as great with any one drug from worker to worker as the variations recorded between the three analogues A cause of this discrepancy in results is possibly due to different definitions of diarrhœa The degree of diarrhœa varies, being in some cases so mild that the patients will not spontaneously use the word "diarrhœa" to describe their symptoms They state that their motions are a little more frequent, usually to the extent of the passage of three or four large soft formed stools in 24 hours "It is not really diarrhœa, it is more like having taken a mild laxative" Putnam et al (1053) on this basis have classified the upset under the two headings of "diarrhœa" and "loose stools", such a distinction is highly desirable We recognised as diarrhœa only those cases in which frequent watery stools were passed accompanied by unpleasant subjective sensations It is important to emphasise that the mere occurrence of diarrhœa has an unfavourable effect on the course of the primary illness (table II), and that it cannot be regarded as an incidental happening even in the absence of pathogenic organisms from the stools

Finland et al (1954) found the incidence of diarrhœa following the administration of these drugs as follows oxytetracycline 19%, chlortetracycline 10%, and tetracycline 4% The incidence of diarrhœa in 108 patients treated with tetracycline by Waddington et al (1954) was 2 cases, and they thought that this was roughly comparable to that previously observed with chlortetra cycline and oxytetracycline Our experience was that the incidence of diarrhœa was roughly comparable in the three analogues, varying between 7% (chlortetracycline) and 12% (oxytetracycline) In the cases treated with tetracycline examination of the fæces in the cases of diarrhœa did not reveal any pathogenic organisms. A similar finding was reported by Reiner et al (1952) in cases of diarrhœa following the administration of chlortetracycline. These workers suggested that a disturbance of the endogenous bacterial flora of the intestine was in itself sufficient to cause diarrhœa possibly by the sheer quantity of metabolites produced by the abundant growth of an otherwise innocent but resistant organism.

Finland et al (1954) observe that the incidence of diarrhœa rises with increasing dosage as in the present series It therefore appeared essential that we should study the serum tetracycline levels achieved with various dosages and the minimum inhibitory concentrations of tetracycline for the commonly encountered organisms

The minimum inhibitory concentrations for the organisms studied were approximately similar to those found by Tunevall and Frisk (1954) but were usually slightly lower than the concentrations found by English et al (1954) From these figures it seems that the aim in treatment should be the achievement of a serum tetracycline level of at least 1·0 µg per ml as soon as possible Our observations on patients on a dosage of 250 mg 6-hourly showed that the serum tetracycline levels rose slowly and illustrated the extreme variability of absorption in different people, as previously shown by Putnam et al (1953) who found that 3 subjects out of 10 had no demonstrable blood tetracycline level up to 6 hours after the administration of a single dose of 250 mg The administration of 250 mg 6 hourly at best produced levels of 0·75–1·00 µg per ml after 10–18 hours

The dosage of 500 mg 6 hourly ensures a more rapid achievement of effective serum tetracycline levels in the first 24 hours but continued administration of this amount leads to an increased incidence of diarrhœa It appears reasonable to use a larger dosage in the first 24 hours and then to continue with the smaller dosage This could be done either as 500 mg 6-hourly for the first 24 hours or as an initial loading dose of 1 g followed by 250 mg 6 hourly the latter method is recommended because of its simplicity and efficiency Using this scheme we achieved a rapid and satisfactory rise of the blood tetracycline levels in the first 24 hours without any increase in the incidence of toxic effects (table III) probably because the increased incidence of toxic effects with the higher doses takes time to develop usually three days The total amount administered in the first 24 hours is 1·75 g., and the serum tetracycline levels at the end of this period agree very closely with those of Tunevall and Frisk (1954) who administered 1·5 g in the first 24 hours

In view of the increasing number of very effective antibiotics now available the claims of any new antibiotic agent must be very critically examined before it is admitted into general clinical usage Tetracycline has at least justified further trial in that the incidence of side-effects appears to be less than that with the other substances of tetracycline series, and it seems to be quite as effective clinically

We wish to thank Dr T H Crozier and Dr J F Pantridge for access to patients under their care Prof G M Bull and Dr M G Nelson for helpful criticism and advice; and Mr H Cox for technical assistance The drug used was 250 mg capsules of Achromycin (tetracycline hydrochloride) provided by Dr A T Mennie of the Clinical Research Department of Messrs Lederle

References at foot of next column

MUMPS MENINGO-ENCEPHALITIS AND THE SERUM-AMYLASE LEVEL

L S WALLMAN
M B Adelaide M.R.A C P D C H
SENIOR MEDICAL REGISTRAR

G L VIDOR
M B Sydney
HOUSE PHYSICIAN

PRINCESS MARGARET HOSPITAL FOR CHILDREN PERTH
WESTERN AUSTRALIA

IT has long been known that meningo-encephalitis may complicate mumps yet its incidence does not seem to be fully appreciated

Patients with meningo-encephalitis usually present with headache vomiting pyrexia and signs of meningeal irritation There may be drowsiness, irritability and focal neurological signs, but the last are extremely rare The cerebrospinal fluid (C S F) shows pleocytosis and contains a normal or a slightly increased amount of protein and an invariably normal amount of sugar and chloride Mumps meningo encephalitis may precede accompany or follow mumps in other sites Occasionally it is the sole manifestation of mumps.

Present Investigation

We have recently studied 25 cases of meningo-encephalitis in a mumps epidemic We could not determine the incidence of this complication mumps not being notifiable in Western Australia but it has been variously reported—from 1·4% (Levison and Thordarson 1942) to 66% (Bang and Bang 1943) The figure given by Bang and Bang refers to the proportion in which there were changes in the C.S F whether or not there was clinical evidence of meningo-encephalitis Candel et al (1944) found in 38 cases of mumps 10 with manifest meningo-encephalitis and a further 20 with pleocytosis of the C S F Eberlein and Lynxwiler (1947) pointed out that mumps meningo-encephalitis could occur alone and found that in 36 of 280 cases no salivary glands were involved

Dunlop (1933) reported that the urinary excretion of diastase was increased in mumps and Candel and Wheelock (1940) showed that the serum-amylase level was raised in 215 of 224 cases of uncomplicated mumps Wolman et al (1947) reported similar results and thought that the serum amylase level did not rise in submandibular and sublingual mumps in the absence of parotitis

In the early phase of the recent epidemic the serum amylase levels were estimated in an attempt to determine the ætiology of meningo-encephalitis in the absence of enlargement of salivary glands The results obtained encouraged us to continue these studies on as many cases as possible

Criteria for Diagnosis

Our criteria for diagnosis were as follows

(1) A history of close contact with a case of mumps within a month of admission

(2) The onset of enlargement of a salivary gland less than fourteen days before or after admission

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DR MCCORRY, DR WEAVER: REFERENCES

English, A. R., P'an, S. Y., McBride, T. J., Gardocki, J. F., Van Halsema, G., Wright, W. A. (1954) *Antibiot. Chemother.* 4, 441
Finland, M., Purcell, E. M., Wright, S. S., Love, B. D. jun., Mou, T. W., Kass, E. H. (1954) *J. Amer. med. Ass.* 154, 561
Helm, W. H., May, J. R., Livingstone, J. L. (1954) *Lancet*, ii, 630
Nelson, M. G., Talbot, J. M., Binns, T. B. (1954) *Brit. med. J.* ii, 339
Putnam, L. E., Hendricks, F. D., Welch, H. (1953) *Antibiot. Chemother.* 3, 1153
Reiner, L., Schlesinger, M. J., Miller, G. M. (1952) *Arch. Path.* 54, 39
Tunevall, G., Frisk, A. R. (1954) *Nord. Med.* 52, 1647
Waddington, W. S., Bergy, G. G., Nielsen, R. L., Kirby, W. M. M. (1954) *Amer. J. med. Sci.* 228, 164
Wood, W. S., Kipnis, G. P., Spies, H. W., Dowling, H. F., Lepper, M. H., Jackson, G. G. (1954) *Arch. in*

ANALYSIS OF 25 CASES OF MUMPS MENINGO-ENCEPHALITIS

Case no	Age (yr)	Sex	Headache	Vomiting	Drowsiness (DR) Irritability (I)	Meningeal irritation	Convulsions	Relation of salivary gland swelling to admission (days)				Abdominal pain (P) Abd tenderness (T)	C.S.F			Serum amylase level (units)	White-cell count (per c mm)	Duration of pyrexia (days)	Remarks
								Before	Simultaneous	After	No swelling		Cells	Lymphocytes %	Protein (mg per 100 ml)				
1	7	M	+	+		+		4				P	450	90	26	500	7500	3	
2	$1\,^{8}/_{12}$	M			DR	+	+			2		P	1100	90	55	174	11 000	3	
3	10	M	+	+	DR	+		2				P, T	400	90	53	410	5000	5	Developed abdominal pain and persistent vomiting for 24 hr 7 days after admission
4	2	M	+	+	DR	+					0		450	90	204	500	4200	4	Slight ataxia on discharge
5	12	M	+	+	DR	+		7				P, T	600	80	74		5500	2	
6	6	M	+	+	DR	+					0		550	95	48	220	6000	4	
7	6	M	+	+		+					0	P	240	90	56	320	8000	5	
8	9	M		+		+		7					130	90	17	500		3	
9	7	M	+	+	DR	+				5		P T	360	90	23	242	10 000	6	
10	12	M	+	+	DR	+				4			300	95	50		7200	5	
11	9	F	+	+		+		7				P T	800	80	39	740	6000	4	
12	3	M	+	+	DR	+			+			P	400	90	50	370		2	
13	6	F	+	+	DR	+			+				320	95	50		8700	3	
14	11	F	+	+	DR	+		14					1000	95	50		11,500	2	
15	4	M		+		+		5					1000	90	60	565		1	
16	10	M	+	+	I	+ +			+				320	95	20	556		6	
17	$1\,^{3}/_{12}$	M		+	DR	+					0		1000	90	33	310	7800	2	
18	6	M	+	+		+			+			P T	320	90	22	416	12 000	4	
19	3	M	+	+		+				2			430	70	20	300	6000	7	Had retention of urine with overflow incontinence for 72 hr
20	9	M	+	−		+	+	7					310	90	84			2	
21	$1\,^{\text{[illegible]}}/_{12}$	M		+	DR	+				1			380	95	50	126	7200		
22	5	M	+	+		+					0		160	95	45	390	5000	4	7 days after admission developed persistent vomiting for 3 days
23	10	M	+	+	DR	+			+				800	90	24	220		4	
24	4	M		+		+		14					350	95	100	285	4100	2	
25	$1\,^{\text{[illegible]}}/_{12}$	F		+	DR	+				1			260	90	21	533 +	7000	3	

(3) Mild meningeal irritation in a child who was not very ill

(4) Sterile C S F with a raised cell count, due mainly to lymphocytes, either a normal or a moderately increased amount of protein, and a normal amount of sugar and chloride

(5) A raised serum amylase level was regarded as additional evidence in favour of mumps as the cause of the meningo encephalitis

5 cases satisfied 4 of the above criteria but did not have definite enlargement of a salivary gland These 5 cases have been included in this report

No facilities were available for isolation of the virus and for serological studies

In this series only children showing signs of meningeal irritation were subjected to lumbar puncture, which was done mainly to exclude the possibility of early pyogenic or tuberculous meningitis

Analysis of Cases

The patients were aged from 14 months to 12 years (see table) There were 21 boys and 4 girls, a finding which corresponds to the sex-distribution reported by Kilham (1949) (80% males), Birnberg (1939) (78% males), and Kravis et al (1951) (83% males)

Headache developed in all except 3 children aged more than 2 years, and vomiting in all but 1 (case 2) Convulsions were present in only 2 patients, 1 of these was an infant aged 20 months (case 2), and the other (case 20) a boy aged 9 years Neither had a history of fits

A history of recent enlargement of a salivary gland was obtained in 9 cases Clinical evidence of mumps was noted for the first time on admission in 5 children, and a further 6 developed typical mumps in hospital 5 children at no stage showed obvious involvement of the salivary glands

Abdominal pain was present in 9 children, of whom 5 had epigastric tenderness

The cell count of the C S F was 130–1100 per c mm, the percentage of lymphocytes being greater than 70 in all cases, and greater than 90 in most of them In only 3 cases was the C S F protein level above 100 mg per 100 ml, average values being 40–60 mg per 100 ml.

Serum-amylase levels were estimated in 20 cases * and found to be raised in 18, 5 of these 18 at no time had *convincing enlargement of a salivary gland* This investigation was made within three days of admission A raised level was still found in 3 cases ten days later

Only 2 children presented focal neurological signs case 4 had mild ataxia, which was still present on discharge seven days after admission, but had disappeared two weeks later, and case 19 developed retention of urine with overflow incontinence which required catheterisation for two days (on leaving hospital, however, his central nervous system was clinically normal)

The raised temperature returned to normal within seven days without treatment in all cases, and no child caused undue concern in hospital

Discussion

The mumps meningo encephalitis observed by us followed the typical benign pattern in the larger series observed by previous workers

Drowsiness was often present, but the patient's active coöperation was readily obtained Vomiting, which was often severe before admission, ceased rapidly in hospital

Lumbar puncture is strongly recommended in all children with signs of meningeal irritation, to exclude early or partially treated pyogenic meningitis A child aged 7 years, who presented a fairly typical history and clinical picture of mumps meningo encephalitis was found on lumbar puncture to have influenzal meningitis which had been treated with antibiotics for twenty four hours before admission In this connection it should be noted that 7 of the 25 cases had been treated with an antibiotic before coming to hospital

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* The method used was based on that of Somogyi (193 0 1 ml plasma or serum was incubated with Somogyi's starch solution, the proteins were precipitated with 10% ZnSO₄ and 0 5*N* NaOH, and the glucose was estimated by the Hagedorn and Jensen blood sugar method (Harrison 1930) The normal range was considered to be 70–200 units The experimental error by this method is ±5%

It is difficult to assess the significance of abdominal pain present in 9 cases; this symptom is common to many pyrexial illnesses in children The possibility of a mild pancreatitis as the cause cannot be ignored

In 18 of 20 cases a raised serum amylase level was found despite the fact that 5 of the 18 had no definite enlargement of the salivary glands either before or after admission The mother of 1 of these 5 (case 17 aged 14 months) had typical mumps three weeks before the onset of her child s illness, and two other members of the family of case 7 developed mumps five days after his admission Wolman et al (1947) stated that, in their experience the serum amylase level did not rise in the absence of parotitis. Our findings do not substantiate this unless one postulates a subclinical parotitis The fact that the serum amylase level is often raised in mumps meningo encephalitis suggests that it may be of value in diagnosing mumps in the absence of the more usual manifestations and in differentiating it from other virus meningo encephalitides, of which the most important is non paralytic poliomyelitis Serological studies with S and V antibodies seldom reach diagnostic titres sufficiently early in the disease to be of great value and only a few laboratories have facilities for isolation of the virus

Summary

25 cases of mumps meningo-encephalitis are reviewed. In 5 of them no enlargement of a salivary gland was detected.

The sex-distribution was 21 males to 4 females

Mild meningeal irritation was invariably present and headache vomiting and fever were the most common associated features

The C.S.F showed pleocytosis and contained either a normal or an increased amount of protein

The serum amylase level was estimated in 20 cases and found to be raised in 18 in 5 of these there was no clinically detectable enlargement of the salivary glands

Serum amylase estimations may be of value in the differentiation of this condition from non paralytic poliomyelitis.

There were no deaths and no sequelæ.

We wish to thank Dr W Seed Dr N Barsden Dr C Lankester and Dr J Watson for permission to publish details of their cases and Miss M McRae for the biochemical investigations.

ADDENDUM

Since submitting this article we have seen 9 additional cases of mumps meningo-encephalitis In 3 of these there was no swelling of the salivary glands and in each the serum amylase level was raised Of the remaining 6 patients 5 had raised levels

REFERENCES

Bang H O Bang J (1943) *Acta med scand* 113 487
Birnberg T L (1939) *Minn Med* 22 173
Candel, S Wheelock M C (1946) *Ann intern Med* 25 88
— — Turk, J I Jun., Smoot J L (1944) *U.S nav med Bull* 42, 661
Dunlop G A (1933) *Lancet* ii 183
Eberlein, W R Lynxwiler C. P (1947) *J Pediat* 31 513
Harrison G A. (1930) Chemical Methods in Clinical Medicine New York.
Kilham L. (1949) *Amer J Dis Child* 78 321
Kravis L. P Sigel M. M Henle G (1951) *Pediatrics Springfield* 8 204
Lenkon, H Thordarson O (1942) *Acta med scand* 112 314
Somogyi, M (1938) *J biol Chem* 125 399
Wolman, I J Evans H Laker S, Jaeger K (1947) *Amer J med Sci* 213 477

Reviews of Books

Pharmacology in Medicine

A Collaborative Textbook Editor VICTOR A DRILL, PH D M.D lecturer in pharmacology Northwestern University Medical School New York and London McGraw Hill 1954 87 sections £7 10s

THIS massive volume looks like the book to end books in the world of pharmacology Each chapter, says the editor has its own numbering of pages and illustrations This he claims, will simplify the editing of future editions and he might have added that it also foxes students and reviewers who share a morbid interest in the number of pages in a book Suffice it to say that Drill weighs 6½ lb which is fair enough for a first-delivery

The reader is introduced easily via physiological considerations, to pharmacology and later to therapeutic applications The ramifications of pharmacology are revealed by substantial contributions on water and salt balance allergic manifestations oral and intravenous feeding and lipid metabolism The text is enlivened here and there with clinical case reports and it is lavishly furnished with references which have a strong American flavour Though comprehensive the book is readable which reflects credit both on the editor and his collaborators The needs of the student and practitioner of medicine are kept constantly in mind only occasionally does the pure pharmacologist take the stage and demonstrate (as some wag has said) not rabbits out of a hat but habits out of a rat The mature student who has learnt to dip judiciously into larger books to supplement his reading will find this volume stimulating but in view of the price most will have to consult it in a library

The book is not faultless in minor matters. The definition of therapeutics— the use of drugs in the treatment or prevention of disease —disregards etymology and gives a much too limited view of the scope of medical care There are some typographical errors, and the attempt using diagrams to equate blood-alcohol levels and their medicolegal significance is an example of over-simplification of a biological problem It fails—as the contributor writing the article is well aware—because it does not take into account the varying susceptibility of the drinkers Philologists will be pained by a reference to " the English slang O.K.

Notwithstanding these small criticisms, this book represents a notable contribution to clinical pharmacology and a milestone in the art of medical editorship

Modern Trends in Blood Diseases

Editor JOHN F WILKINSON M D M.SC PH D F R C P F R.I C. director of the department of hæmatology Manchester Royal Infirmary London: Butterworth 1955 Pp 359 65s

AUTHORS in this series are actually engaged in the work written about and are encouraged to state their own views and results rather than to attempt a comprehensive review of published work Most of those contributing to this volume have produced readable essays and deadly summaries with rows of references have been avoided by almost all The editor has naturally gathered contributions from his colleagues in Manchester but he has not limited himself to Manchester or even to this country and there are three first-class transatlantic contributions

D Ll Griffiths has an original and very well illustrated chapter on bone changes in blood-diseases. M C G Israëls gives a succinct account of his ideas on the classification and treatment of reticuloses, and a well reproduced colour plate shows histological and blood changes The chapter on skin changes in blood-diseases by J H. Twiston Davies collects together a lot of scattered and much new information and the same can be said about D B H Dawson s chapter on changes in the fundus in blood diseases F Stratton has an interesting chapter on the occurrence detection, and avoidance of iso-immunisation to blood group antigens, including all the newer groups The chapter on hæmolytic anæmia by Crosby and Dameshek is a remarkably clear thoughtful and concise account of our present knowledge of this difficult group. Carl Moore and R Dubach compress into 25 pages an account of how our ideas on iron metabolism have been changed by using *radioactive iron*, and Cartwright and Wintrobe give a notable account of their researches into iron, copper, and porphyrin metabolism in the anæmias that accompany infections W F Gaisford, writing on hæmatology in childrens' diseases, C Rimington on pigments and porphyrins, and C C Ungley on vitamin B_{12} and megaloblastic anæmia, survey their respective fields Alexander Brown gives a short account of anticoagulant therapy, its indications, its control, and the drugs to use, this is the only contribution in the field of blood clotting studies, perhaps because comprehensive accounts of present researches and ideas have been published only recently Finally, the editor and his co workers deal with the treatment of chronic and acute leukæmias in two chapters which, despite the inevitable delays of book production, are notably up to date

Anyone contemplating research on any of these subjects should read the relevant chapter first, the contents list shows how much of interest there is for specialists in other fields too

Advances in Virus Research

Vol II Editors KENNETH M SMITH, virus research unit, Molteno Institute, Cambridge, MAX A LAUFFER, department of biophysics, University of Pittsburgh, Pennsylvania New York and London, Academic Press 1954 Pp 312 $7 00

THE editors point out that their second instalment needs to be taken with volume I for a proper balance Certainly volume II wears a much more physicochemical look than its predecessor, and one or two of the articles are written by the initiated for the initiated

There is, however, an extremely fine assessment of electron microscopy of viruses, by R C Williams Electron microscopy has been called the science of artefacts, and Williams's article, written with a biological slant, is a careful attempt to separate the facts from the artefacts W W Ackermann and T Francis write about viral development in tissue cultures, mainly an account of the interesting work from their own laboratory on the effects of various chemical inhibitors on different stages of viral development within cells P von Magnus's chapter on incomplete forms of influenza virus is incomplete in some respects C A Knight gives a very useful review of the chemical constitution of viruses, with pride of place to the plant viruses F O Holmes and F C Bawden discuss plant diseases and inheritance of resistance to viral diseases in plants and inhibitors E Pollard and M A Lauffer and I J Bendet deal with the action of ionising radiation on viruses and the hydration of viruses respectively

The new volume contains less about animal or bacterial viruses than some readers would like, but no doubt the balance will be restored in volume III

Die Tests in der klinischen Psychologie

Erster Halbband Editor Prof Dr ERICH STERN Zürich Rascher 1954 Pp 418 Sw Fr 28 10

DURING the last twenty years there has been a comparative dearth of original work and publications on psychological tests in the non-English-speaking countries In his introductory chapter Professor Stern, editor and chief contributor of this volume, comes to the conclusion that clinical psychology requires the use not only of tests but also of history-taking, clinical observation, and interviews

His exposition and that of several other contributors shows a medical bias which perhaps accounts for the weak technical treatment of test procedures and their validation By modern standards, many of the chapters are superficial on this point, though informative about the empirical use of the tests Other chapters are, however, sophisticated—e g, Hathaway and Meehl's brief account of the Minnesota personality inventory After a general review of history and problems, there are a number of chapters on intelligence and performance tests, the development of children, the study of motor behaviour, and statistical methods, including factorial analysis The second half of the book describes personality tests, especially the M M P I, Eysenck's attitude inventory, Jung s association tests, and the procedures of Szondi, Mira, and Tramer In a second volume (which it is promised will contain the index which the reader lacks when consulting this volume) further personality tests will be considered as well as vocational tests. The two volumes are to be the opening portion of a system of clinical psychology, edited by Professor Stern. It may be predicted that it will be to a large extent a system of psychological medicine

Surgery of the Small and Large Intestine

CHARLES W MAYO, M D, section of surgery, Mayo Clinic, Rochester, Minnesota Chicago Year Book Publishers London Interscience Publishers 1955 Pp 340 68s

"INTESTINAL surgery without tears," might be the subtitle, since this work is concerned with operative technique portrayed by line drawings facing almost every page of text It is not a profound work, being written by the practical man for the less practised man the author explains in the preface that it is no part of his task to refer to the literature

Details of technique are occasionally expanded with words of advice and general experience, not without charm "My father remarked long ago that, except for resection, one should avoid touching the intestine affected with ulcerative colitis just as one would avoid touching the roof of an old tent without a fly in a rainstorm" In general the advice is sound though some eyebrows will be raised at the statement that for intussusception, whether reducible or not at the time of operation, resection is as a rule indicated because of the tendency of the condition to recur There is a useful preliminary chapter on diets, and another on methods of intestinal anastomosis, it is good to find the author advocating not only end to-end anastomoses, even when ileocolic, but also the open technique

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Diseases of the Nervous System (8th ed Edinburgh and London E & S Livingstone 1955 Pp 357 24s)—Sir Francis Walshe, F R S, has had the satisfaction, in the eighth edition of his widely used textbook, of shortening the chapter on neurosyphilis—once the most prominent cause of disorders of the nervous system He has always taken the opportunity offered by new editions to examine much that is new, and—of necessity—some that is ephemeral, for, as he says in his latest preface, only thus can an author fulfil his responsibility for stimulating the critical thinking of his readers

Diseases of Infancy and Childhood (7th ed London J & A Churchill 1955 Pp 804 50s)—In Dr Wilfrid Sheldon's well known book, interesting signs of the times are the omission of the section on wet nursing and the cautious but partial approval of demand feeding—contrasting with the uncompromising adherence of previous editions to rigid feeding schedules The author's strong views on the toilet training of infants will not meet with everyone's approval The omission of the section on flatulence and colic from the chapter on digestive disorders of infancy is curious, for infantile colic remains as common and troublesome as ever and it has been much discussed in recent years There are fewer prescriptions in the new edition now that many more specific remedies are available, and the appendices on dosage of drugs and on sulphonamide and antibiotic therapy have been removed. There are many new illustrations mainly of excellent quality, but one or two of the older blocks are getting just a trifle worn Despite much new material this edition is eight pages shorter than its predecessor Students will find it as good a friend as ever

Human Adrenal Cortex.—Volume VIII in the Ciba Foundation Colloquia on Endocrinology reports the proceedings of the conference on this subject held at the foundation last year in two parts The first, under the chairmanship of G Pincus, covered histological and biochemical aspects and corticomedullary relationships, the second, under the chairmanship of G W Thorn, dealt with physiological and pathological aspects and with hypothalamic and pituitary relationships The editors of the volume are Dr G E W Wolstenholme and Miss Margaret Cameron (London J & A Churchill 1955 Pp 665 55s)

Gestation—The Josiah Macy, jun., Foundation New York, has published the transactions of the conference on this subject held in March, 1954 The editor is Prof Louis B Flexner, M D (1955 Pp 238 $5)

THE LANCET

LONDON SATURDAY MAY 28, 1955

Surgical Treatment of Parkinsonism

THE search for effective measures to control parkinsonism continues The latest operation involves occlusion of the anterior choroid artery [1 2]—a measure suggested by relief of tremor and rigidity in a patient with parkinsonism after accidental tearing of this artery during the approach to cerebral pedunculotomy COOPER [2] has occluded the vessel by clips and diathermy through a subtemporal approach In 30 such operations the mortality was 13% Apparently the most constant effect is relief of rigidity which is striking Moreover in 9 of the 11 postencephalitic cases tremor has been eliminated or materially lessened for periods of, so far, up to a year In these first 30 cases there have been only 2 instances of postoperative hemiplegia due apparently to an effect on the middle cerebral artery, and there have been 3 instances of transient palsy of the oculomotor nerve The postencephalitic group did best of all Neither of the 2 arteriosclerotic cases which were operated on survived.

The introduction of this operation has given rise to a good deal of discussion about the anatomical distribution of the anterior choroid artery and the accuracy of efforts to occlude it ABBIE [3] had previously drawn attention to variations in the course and distribution of the artery and to its anastomosis with the posterior choroid vessels and CARPENTER et al [4] have now found from necropsy studies that in only just over three quarters of 60 dissections did the artery arise from the internal carotid artery They confirm that it is usually the first branch to be given off after the posterior communicating artery, but in 10% of cases other lenticulostriate vessels intervened Moreover the branches of the anterior choroid artery itself varied in their origin, and in half the cases the first branch arose 5–10 mm along the parent trunk Thus it may be difficult to ensure that the anterior choroid artery is the one that is clipped, and even when, as COOPER recommends, diathermy is applied along the artery in order to prevent collateral circulation the blood supply to the globus pallidus may remain intact COOPER has done bilateral angiography before operation in order to determine the position of the vessels, but this method is unlikely always to show these fine vessels with sufficient accuracy The anterior choroid artery may have a wide area of distribution but all the evidence suggests that it constantly supplies the globus pallidus and the presumed rationale of the operation is that it produces ischæmia or infarction of this structure In this series there was no example of a visual field defect or hemiplegia resulting from occlusion of this vessel. But in the clinical syndrome of occlusion of the artery [3] hemiplegia is constant from impairment of the blood supply to part of the posterior limb of the internal capsule, and a field defect is common from involvement of the blood supply to the optic tract or radiation or the lateral geniculate body This adds to the difficulty of accepting the explanation of the operative results, unless one assumes that the globus pallidus has a relatively poor blood-supply or that in a diseased state it is particularly vulnerable to partial ischæmia.

Nor are the uncertainties only anatomical The exact mechanism of the rigidity and the tremor is far from clear—as is shown by the variety of the surgical approaches On the one hand some assume that these disturbances result from disordered function of the globus pallidus, and this may be countered by destroying it through interference with its blood supply (COOPER's operation) by direct electrocoagulation using stereotaxic procedures,[5–7] or by division of its efferent-fibre connections with the thalamus through section of the ansa lenticularis and fasciculus lenticularis [8] and NARABAYASHI and OKUMA [9] report from Japan excellent results from injecting procaine in oil into the globus pallidus Others, on the other hand believe that the movements must originate in the motor cortex and seek to relieve tremor by excising part of this cortex or by interfering with the motor projection, at the cost of hemiparesis Excision of the motor area [10] partial division of the anterior limb of the internal capsule [11] cerebral pedunculotomy,[12] and cordotomy [13–15] are all practised, although rigidity may be little relieved and may even be accentuated There is a third approach Some patients with parkinsonism are much worse under emotional stress and OLIVER [15] has helped some of these patients by selective frontal leucotomy (undercutting areas 6 8, 9) Apparently similar results in the wider field of motor disturbances are being obtained by TAKEBAYASHI [16] BROWDER has drawn attention to frontal lobe symptoms after his capsule operation, and we do not know enough of the connections of the corpus striatum to exclude indirect frontal lobe effects from operations directed at the globus pallidus.

The usefulness of surgery in parkinsonism is necessarily limited for the results are best in the younger patients, and in those where the symptoms are predominantly unilateral and the signs more or less stationary whereas usually the disorder affects older people and is bilateral and progressive For a year or so after most of these operations the patient may benefit by having exchanged tremor for hemiparesis, but later on when the disease has progressed, the sequelæ of the operation are apt to become an added disability COOPER's operation on the anterior choroid artery is especially interesting because it apparently relieves rigidity as well as tremor, and because it may

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Cooper I S *Science*, 1953 118 193

Cooper I S *Surg Gynec Obstet* 1954 99 [illegible]

Abbie A A *Brain* 1933 56 233

Carpenter M B, Noback C R, Moss M L *Arch Neurol Psychiat* 1954 71 704

[5] Spiegel E A Wycis H T Thur C *J Neurosurg* 1951 8 452

[6] Talairach J de Ajuriaguerra J David M *Pr méd* 1952 60 605

[7] Fenélon F *Sem Hôp Paris* 1952 28 3775

[8] Meyers R N Y St J Med 1942, 42 317

[9] Narabayashi and Okuma *Psychiat et Neurol Jap* 1953 p 61

[10] Bucy P *Amer J Surg* 1949 75 257

[11] Browder J Kaplan H A Rabiner A M *Ann Surg* 1953 138 601

[12] Walker A E *Acta psychiat Kbh* 1949 24 723

[13] Putnam T J *Arch Neurol Psychiat* 1940 44 950

[14] Oliver L C *Lancet* 1950 i 847

[15] Oliver L C Parkinson's Disease and its Surgical Treatment London, 1953

[16] Takebayashi *Med J Osaka Univ* 1951 2 1

be applicable to bilateral cases Electrocoagulation of the globus pallidus by means of stereotaxis also has these potentialities, but this method is likely to be used in only a few highly specialised centres

As long as our knowledge of the basic anatomy, physiology, and pathology remains incomplete, firm conclusions on the rôle of surgery will be difficult to make But undoubtedly many patients have been helped by one or other of these operations

Children in Hospital

For better or worse we are competitive animals, goaded to our best efforts chiefly by observing the achievements of others Thus it is an important duty, in any discipline, to see—or, failing that, to hear—how the other fellow does it Young children, admitted to hospital, are so prone to suffer a setback in their emotional development that people in many countries are now seeking to prepare them for, or protect them from, the risks of this particular experience, but attempts have been scattered and piecemeal, and it has not always been easy, or perhaps even possible, for those who minister to a child's physical needs in hospital to pay more than lip service to the requirements of his psyche A study group of the World Health Organisation have been examining the problem, and an account of their findings, by Dr Mary Capes,[1] has now appeared The group was composed of distinguished physicians, pædiatricians, and psychiatrists from the United States and fourteen European countries, and the report shows how remarkably the outlook in these various countries differs, even though they all have a common tradition

The members of the group agreed—as most others will—that a sick child is usually best off in his own home, and that many more children could be treated there if some additional services were provided to help the parents In some countries, our own among them, both parents may go out to work, and a child may be admitted to hospital for this reason alone The group suggested that firms employing women should maintain a relief staff, who could take over the work of a mother absent because of the sickness of a child They also thought that the mother should receive sickness benefit for the child equivalent to the wages lost, so that she would not be tempted to put her job before her child Sometimes a child who is making little progress as an outpatient is admitted by the pædiatrician merely because he is at a loss what to do next He should make it clear—at all events to himself—why he wants the child in and what investigations he intends to do, and he should be convinced of what the study group called "the unconditional necessity" of the step In some countries—or rather at some hospitals in some countries—thought is being given to preparing the child for admission This is not an easy thing to do, especially with children below the age of 4 or 5, for they often take what is happening to them to be a punishment, and accept with terror the idea that their parents have rejected them A young child, unless his physical condition compels it, should never be sent into hospital just before or just after the birth of his successor in the family Emergencies are a different matter then the parents as well as the child need emotional support, and they should be allowed to stay near the child and, particularly, to be with him when he comes round from an anæsthetic In some hospitals the pædiatric department has a playroom, staffed with "play nurses", and here the convalescent child can "play out" his experiences and so reduce the anxiety they have provoked In some hospitals parents are given a booklet advising them on the way to prepare their children for admission, and in others—including some in this country and in New Zealand—the mother is admitted with the child, and not only keeps him company throughout his stay, but does all her usual services for him, and even, under guidance, all his dressings The benefits obtained from this practice by Cecily M Pickerill and H P Pickerill[2] in New Zealand have not been psychological only nursing by the mother has also cut out *all* cross infection in a hospital engaged in plastic repairs of hare lip and other developmental anomalies

There are some pædiatricians—and some parents too, the group report—who believe that in a hard world children should be toughened from birth onwards Some hospitals, too, take the view that it is not much use worrying about the effects of hospital experiences on children so long as there are child psychiatrists and child-guidance clinics to look after casualties, they must just take their chance The need for prevention of such casualties is thus evaded, not merely because of the pressure of clinical work but almost as a matter of policy A wasteful policy, surely, for though no-one can live his life without experiencing difficulties and struggling to overcome them, the initial tolerance of young children to such stresses is low, and, as the study-group say, the dosage must be graded if they are to avoid permanent damage Hence they emphasise the importance of the mother's presence when the child is in hospital she is the most effective prophylactic we have against psychic trauma, because she provides the normal emotional environment of the child

Physical environment, too, deserves some thought The group pointed out the drawbacks of both old high wards and new glass cubicles ("conveying the impression of a refrigerator")—though they recognised, of course, the value of isolation. The wards, they say, should be small, with a cot like the one the child is used to at home, and "with furnishings he will appreciate", and he should not, at the moment of admission, be deprived of his toy from home or his own clothing At no stage should he be subjected to routine procedures which are not really necessary, or alarmed by syringes and preoperative enemas, or allowed to get to the anæsthetic room in a state of frightened awareness

Among unnecessary routine procedures must be classed the too rigorous limitation of visitors The group noted that in Italy, where people are traditionally warm-hearted to children, visiting has never been forbidden, and the only exceptions made are in cases where visiting seems likely to cause serious harm to the child In East Africa the child's mother, or some other relative, and indeed often his whole family, camp at his bedside day and night, and the main difficulty is to prevent the mother from taking the child out of bed to sleep beside her on the floor, or from getting into bed beside him The member

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ne Child in Hospital *Bull Wld Hlth Org* 1955, 12, 427

[2] *Lancet*, 1954, i, 425 see *Ibid* p 447

the study group who reported thus found it had given him food for thought, for there appeared to be less evidence among these children of psychological disturbance Though no statistics are available to show whether in fact they do have less psychological trauma as a result of the upheaval than do European children, the possibility is interesting The group note that ' there are still many children s hospitals in a number of countries where visiting is forbidden, and many others where it is grudgingly permitted once weekly or even less '—no doubt because the fear of cross infection has been magnified out of proportion to its importance The British Pædiatric Association in 1945 analysed data collected in twelve different centres and concluded that there was no positive evidence that visiting *by adults* increased infection it is the presence of other children which introduces risks Children making a long stay in hospitals or institutions are specially prone to suffer an arrest in emotional development and many of the group felt that parents should be allowed travelling expenses to visit such hospitals especially those remote from towns Children in such long stay wards who never get visited suffer bitterly and should be a special concern of the pædiatrician and nurses Where there are play nurses on the staff they can be encouraged to spend extra time with such lonely children

The group gave much thought to the training of staff for children s departments how far should the pædiatrician be a psychiatrist, or the psychiatrist a pædiatrician, and how far should the nurse be familiar with the work of both ? An extensive course offered in his university was described by one of the members Dr M J E SENN professor of pædiatrics and psychiatry at Yale

> The emphasis is on growth and development behaviour and the parent-child relationship A pædiatric residency lasts two to three years, and one method used is to introduce the young pædiatrician to life outside the hospital : each intern on starting follows the last three months of pregnancy in a woman who agrees to accept him as her pædiatrician He gets to know the family witnesses the birth sees the mother's response to labour and to the child meets both in the well baby clinic, and is called into the home if at any time the child falls ill He works under an assistant resident and if special problems arise can call in a senior member of the staff in consultation At case-conferences, attended by the whole staff patterns of growth in behaviour in the children attending the department are discussed The aim is always to bring out the mental as well as the physical aspect of each case

Similar training schemes were reported from a few other countries and the group thought the principle sound They recommended that pædiatricians should be trained in those children s hospitals where it is possible for them to work with a psychiatric team , or failing that should spend at least a year in a child guidance clinic Similarly they felt that the child psychiatrist should have carefully planned training in pædiatrics They took a serious interest, too in the training of the pædiatric nurse and here again the experience of Yale was illuminating In addition to lectures and discussion groups on pædiatrics and the physical care of children, nurses too are taught growth and development as part of their practical training Thus they spend two weeks in a nursery school and two weeks as a ' play nurse working with a full time ' play worker in the wards They join the medical rounds and are encouraged, as members of the team, to ask questions , and they attend a weekly conference of student and graduate nurses with the pædiatrician They are also warned of the stresses and pitfalls of their job—the risks of becoming too possessive, of resenting the real mother, and of becoming impatient with a child who regresses to behaviour patterns too young for his age

The W H O report is a plea for close collaboration between the pædiatric and the psychiatric teams only by working together can they arrive at a balanced diagnosis, and so plan treatment to protect and heal the whole child

Annotations

GENETIC FACTORS IN EPILEPSY

EPILEPSY is not an easy subject for genetic study fits can be caused in many different ways and it is difficult to decide which of several possible factors is at work In the last few years each of the more obvious lines of approach has been carefully explored Alström[1] divided his index cases according to whether the ætiology was known probably known or unknown He found no striking differences between the risks to the relatives in each of these three groups But as Alström says

> It is never possible to determine the causal connection other than with varying degrees of probability

Harvald[2] following Lennox[3] divided his index cases by their electro encephalograms He was fully conscious of the limitations of this method but all the same found it gave some interesting results Ounsted[4] working entirely on children, has classified his index cases purely by their clinical features and then noted the groupings suggested by the pattern of fits in the near relations

Excluding all cases of infantile convulsions alone, Harvald found, in common with earlier workers that the risk to first-degree relations of developing epilepsy was from $2^1/_2$ to $4^1/_2$% The risk was less when the electro encephalogram of the index case was normal or near normal than when it was definitely abnormal This was true whether the abnormality was of the 3 per second ' spike and wave pattern or of the 3 per second paroxysmal pattern or showed a well-defined focus He found like Lennox that the electro-encephalograms of the relations were much more often abnormal than were their clinical histories and that the abnormality tended to be of the same type as that of the index case The exception to this was that the relations of index cases with focal abnormalities in the electro-encephalogram showed no increase in abnormal electro encephalograms of any kind even though they had an increased incidence of epilepsy He also found that ' carriers who had probably transmitted epilepsy though themselves unaffected, often had normal electro-encephalograms Harvald suggests that a tendency to cerebral paroxysms and a tendency for these paroxysms to develop into fits are inherited independently and that several genes are concerned

Only a preliminary report of Ounsted s very extensive survey of children in the Oxford district has so far been published His purely clinical approach has much to commend it He included among his index cases all children who had had convulsions of any kind and divided them in the following way remittent febrile convulsions febrile convulsions continuing until death febrile convulsions associated with a brain infection, epilepsies which remit epilepsies which resist treat ment and persist, febrile convulsions which are followed by epilepsy which then remits, febrile convulsions which are followed by persistent epilepsy, and a mixed group of other convulsive disorders such as anæsthetic seizures. Any convulsions among the brothers and sisters of the index cases were classified in the same way, and so in each group there was drawn a family pattern of convulsions of the different types. In this way the group of index cases with remittent febrile convulsions, remittent epilepsy, and convulsions followed by remittent epilepsy were found to have much the same family pattern. The sibs showed a high incidence (17–25%) of convulsions of all types, most of these being remittent convulsions and about a third epilepsy. The epilepsy was most often remittent epilepsy, or convulsions followed by remittent epilepsy. The sibs of the index cases with continuing epilepsy showed about the same amount of convulsions of all kinds and of epilepsy (9%) but the epilepsy here in most instances was continuing and resistant to treatment, like that of the index case. In contrast to both these was a family pattern found with convulsions associated with brain infection, encephalitis, or meningitis. Here the sibs had an incidence of convulsions of all sorts of 6% and of epilepsy of only 2%; most of the epilepsy was of the continuing type. This pattern may well be that of any random sample of children. Thum [5] did in fact find an incidence of 6% of convulsions in a group of over three thousand children in Boston, Massachusetts. Two other groups were of special interest. First, the group of children in whom the convulsions went on continually until they died might perhaps be expected to behave like the group with brain infections; but the incidence of convulsions of all sorts in the sibs was nearly 30% and the incidence of epilepsy nearly 17%, most of this epilepsy being of the continuous type resistant to treatment. The other group of special interest were the children with temporal lobe attacks, often assumed to be purely symptomatic. Here the family pattern was very much that of groups where the index cases had remittent febrile convulsions or remittent epilepsy, with 15% of convulsions of all sorts and 6½% of epilepsy, most of which was remittent epilepsy. Genetic endowment would appear to play a part here too. This has of course no direct bearing on the value of surgery for this disease.

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[1] Alström C H Acta psychiat Kbh. 1950 suppl. 63
[2] Harvald B Heredity in Epilepsy Copenhagen 1954
[3] Lennox W G Amer J Psychiat 1947 103 457
[4] Ounsted C Eugen Rev 1955 47 33

A possible interpretation of these findings in children is that one genetic factor or group of factors predisposes to remittent febrile convulsions or remittent epilepsy, or sometimes temporal lobe epilepsy; while another factor or group of factors predisposes to persistent epilepsy resistant to treatment but sometimes results only in remittent febrile convulsions. Febrile convulsions continuing till death would then appear to be due to an intense form of the second group of factors.

NEW STEROIDS

COMPARATIVELY minor alterations in structure can profoundly change the pharmacological characteristics of a steroid hormone. Thus a halogenated derivative of hydrocortisone, 9α-fluorohydrocortisone, exerts a much greater anti-inflammatory action, weight for weight, than hydrocortisone, and in terms of mineralocorticoid activity it is proportionately even more potent. Because it readily brings about sodium retention, this compound is unsuitable for use in the treatment of rheumatoid arthritis.[6] There would be an obvious place for substances suppressing inflammation without inducing sodium retention; and it has been claimed that two new synthetic steroids—metacortandralone and metacortandracin—meet this need.

Bunim et al.[7] found from the administration of metacortandralone to seven patients with rheumatoid arthritis that it was three to four times more potent than cortisone, and two to three times more potent than hydrocortisone. Effects on the clinical picture, the erythrocyte sedimentation rate, and C-reactive protein were similar to those of cortisone. With doses which effectively suppressed the signs of active arthritis, there was no sodium retention or potassium loss. With rather higher doses a negative nitrogen balance developed. The steroid did not raise the fasting level of blood sugar, and in no case did glycosuria appear. The undesirable effects, described as minor, included manifestations of Cushing's disease seen in some patients treated with cortisone—hirsutism, facial rounding, acne—and also sleeplessness and transitory mental depression. Hypertension did not develop. The properties of metacortandracin were very similar. Bunim and his colleagues emphasise that there is still no information about the effects of long-continued administration of these new steroids.

Metacortandralone and metacortandracin may prove useful in cases where cortisone produces excessive sodium retention. But probably many of the limitations of cortisone are shared by these new derivatives—there is, for example, little reason to hope that in rheumatoid arthritis they will arrest damage to the joints any more effectively. In further trials the suppressive effect of these derivatives on the adrenal cortex will have to be assessed.

DEFORMITY OF THE PYLORIC ANTRUM

THE most important cause of persistent deformity of the pyloric antrum is carcinoma; but benign lesions of the stomach or duodenum or, occasionally, extrinsic causes can give rise to very similar radiographic appearances. Balint and Slater [1] point out that no single diagnostic measure—clinical examination, radiography, gastroscopy, or even laparotomy—can be relied on to distinguish the benign from the malignant lesion. Gastroscopy and radiography are complementary methods of examination [2]; some, such as Flood and Hennig [3] emphasise the limitations of gastroscopy but others have found it very reliable. Radiography is the simplest method of demonstrating antral deformities, but its value depends very largely on the individual radiologist. Even in expert hands, it does not always reveal clearly whether an ulcer is benign or malignant.

Allen and Welch [4] estimate that of all prepyloric ulcers 75% are malignant; but Ransom [5] found that in his series some 90% were benign. The gastric ulcer—particularly at the antrum—that shows no signs of healing despite clinical improvement should be regarded as possibly malignant. On the other hand, apparent healing does not exclude malignancy. Gastric analysis may be helpful, in that the absence of free hydrochloric acid is commoner in carcinoma than in benign lesions; but gastric carcinoma can exist in the presence of hyperchlorhydria.[6]

In some cases of antral deformity no cause can be demonstrated.[1] Flood and Hennig studied 42 cases of "benign antral disease," in 9 of which no evidence of ulcer was brought to light. Possibly the deformity is sometimes due to true antral gastritis, and in one of the cases reported by Balint and Slater there was histological evidence of "chronic gastritis"; but many radiologists hesitate to make such a diagnosis, particularly since it is commonly not easy to confirm. Possibly, as Balint and Slater suggest, in other cases the deformity is the outcome of recurrent peptic ulceration with persistent spasm or residual scarring of the antrum; and occasionally per tent spasm develops in the apparent absence of any al disease [7]

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[5] Thum D A *Amer J Psychiat* 1942 98, 574
[6] Boland E W Headley N E *Ann rheum Dis* 1954, 13 291
[7] Bunim J J, Pechet M M Bollet A J *See Ibid* 1955, 14, 33

[1] Balint, J A, Slater, J D H *Gastroenterologia, Basel* 195[illegible] 6 330
[2] Benedict E B *Gastroenterology*, 1947 8, 251
[3] Flood C A, Hennig, G C *Ibid*, 1951 19 787
[4] Allen A W, Welch, C E *Ann Surg* 1941, 114 498
[5] Ransom H K *Ibid* 1947, 126 633
[6] Avery Jones F *In* British Encyclopædia of Medical Practice London, 1952 vol 11, p 581

When the radiographic or gastroscopic appearances are onclusive, laparotomy is preferable to a policy of it and-see But laparotomy also has its limitations ulcer or early malignant infiltration is not always tectable and a malignant ulcer may appear benign d an inflammatory mass around the duodenum lignant[7] so sometimes the diagnosis can be ablished only by microscopic examination

ADENOSINE AND THE HEART

Drury in 1936[8] described detailed studies of the tion of adenosine derivatives on the heart in small imals The main effect was on the conducting system th sinus slowing and auriculoventricular block. Green d Stoner[9] found that these compounds also caused a nsient fall in blood pressure Honey et al[10] showed at adenosine could produce heart block in healthy n The effect of magnesium adenosine triphosphate the electrocardiogram (E.C.G.) was extensively studied Wayne Goodwin and Stoner[11] in patients who were ceiving intravenous injections of this substance as eatment for rheumatoid arthritis When the injection s made rapidly there was invariably subjective dis rbance consisting of hyperpnœa, cough, flushing and transient sensation of faintness In all cases the blood essure fell the greatest reduction being by 100 mm. Hg e changes in the E C G were remarkably constant nall doses (5–15 mg) produced brief sinus bradycardia llowed by sinus tachycardia Larger doses (15–30 mg) used pronounced sinus slowing, and in addition pressed the conducting tissues with consequent first second degree auriculoventricular block, Wenckebach riods and occasionally complete asystole for several conds The action of adenosine was similar to that of enosine triphosphate but less distinct The production auriculoventricular block by adenosine triphosphate as prevented by atropine indicating that this action as mediated through the vagus Adrenaline produced similar effect to atropine The action of adenosine iphosphate on the heart was not confined to the nducting tissues ; alteration in the ST segment and entricular ectopic contractions suggested a direct effect n the myocardium. These myocardial effects were found be decreased by the magnesium ion which potentiated e depressant action on the conducting system

Adenosine triphosphate also brings about dilatation of he coronary arteries in animals[12] and various forms of denosine have been used from time to time in the reatment of cardiac and peripheral vascular disease Vayne Goodwin and Stoner[11] considered that use of his substance for such purposes might be unwise in iew of the direct effects on the myocardium while Honey et al[10] did not regard adenosine as useful for he treatment of heart-disease In a letter on p 1125 r Somló describes the treatment of supraventricular aroxysmal tachycardia by rapid intravenous injection adenosine triphosphate 20 mg Both the subjective ffects and the E.C.G changes were essentially similar to hose described previously, except that there was nvariably ventricular asystole sometimes followed by ultifocal ventricular ectopic beats which in turn were ollowed by normal beats and then by normal sinus ythm There were no untoward side-effects

Adenosine triphosphate may prove a powerful thera utic weapon against paroxysmal tachycardia But it ould be remembered that supraventricular tachycardia is often a benign condition which is a nuisance rather than a danger and that attacks commonly terminate *spontaneously Most physicians therefore prefer first* to try simple measures such as carotid pressure or trick manœuvres to induce vagal stimulation sedation or oral administration of digitalis But not all cases respond to such treatment and long-continued paroxysmal tachycardia may constitute a real danger to the patient In such circumstances adenosine triphosphate might certainly be considered and this drug may be more effective than others such as methacholine chloride quinidine or procainamide, which are not uncommonly used Adenosine triphosphate might with advantage be given as the magnesium salt which has less direct action on the myocardium.[11] In view of its action on the myocardium, great caution is necessary in administering it to patients with organic heart disease and much cardiac enlargement but need to terminate the ectopic rhythm may justify the risks. Adenosine triphosphate should not be given without E C.G control and preferably atropine should be at hand in case prolonged asystole ensues It seems possible from Somló s observations that adenosine triphosphate might induce ventricular tachycardia but this has apparently not arisen on any of over four hundred occasions referred to by Dr Somló when the drug was administered to terminate a supraventricular paroxysm of tachycardia

Somló considers that the response of supraventricular tachycardia to adenosine triphosphate is so specific as to constitute a diagnostic criterion But of course as he would no doubt agree, the diagnosis should be established clinically and electrocardiographically before the drug is administered

A SNOW CENTENARY

EPIDEMIOLOGISTS have been accused of having a Broad Street Pump fixation which blinds them to the needs and opportunities of work on diseases of more immediate importance than cholera Quite unabashed, the section of epidemiology and preventive medicine of the Royal Society of Medicine met on May 17 at the London School of Hygiene and Tropical Medicine to celebrate the centenary of the publication of Dr John Snow s classic *On the Mode of Communication of Cholera* A group of students working for the diploma in public health had prepared an exhibition (which will be open for a month) of Snow miscellania ranging from a hitherto little-known portrait painted at the request of Queen Victoria to an account of the findings at necropsy after his tragically premature death from chronic renal disease at the age of forty five The exhibits outline the main facts of his life and the steps which led him to record his belief that cholera was spread through infection of the community s drinking water by the patients dejecta first rather tentatively in 1849 and then with forceful conviction in the more substantial edition of 1855 This book which as Wade Hampton Frost said in his introduction to the Commonwealth Fund reissue should be read once as a story of exploration and many times as a lesson in epidemiology is indeed the exemplar of the epidemiological method at its best

Prof A Bradford Hill F R.S the section s president pointed out that Snow had to wait for confirmation of his thesis until the disastrous epidemics of the 1850s when the removal of the intake of water supplied by the Lambeth Company up the Thames to Ditton produced the remarkable contrast in cholera mortality which formed the basis of Snow s experiment on the grandest scale In Southern London the pipes of both the Lambeth Company and the Southwark and Vauxhall Company (which drew the filthiest stuff ever drunk by a civilised community from the Thames in the heart of the city) went down every street supplying rich and poor clean and dirty in a manner which had all the

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Jenkinson, E. L., Hammerrick F J *Radiology* 1948 51 708
Drury A N *Physiol Rev* 1936, 16 292
Green H N, Stoner H B Biological Action of the Adenine Compounds London 1950
Honey R M, Ritchie W T Thomson W A. R *Quart J Med* 1930 23, 485
Wayne E. J., Goodwin J F Stoner H B *Brit Heart J* 1949 11 55
Drury A N Szent-Györgyi A *J Physiol* 1929 68 213

appearances of random allocation Yet, as Snow found out by arduous "shoe leather epidemiology," the absolute number of deaths in the houses supplied by the Southwark and Vauxhall Company was vastly greater than among the customers of the other Unfortunately, he did not then know the number of houses supplied by each company in the area, and could not give his dramatic contrast the rigorous basis which only comparable rates provide, until a year after the publication of this main work Meanwhile, the epidemic centred round the pump in what is now Broadwick Street had exploded with appalling results Within three days over three hundred people were dead from cholera The dramatic account of Snow's discovery of the focal importance of the pump and his appearance before the local vestry to recommend the removal of the pump-handle is well known But Snow himself shunned the facile argument that the epidemic was thereby halted, and indeed he pointed out that the panic stricken flight of the inhabitants had already done that by what would now be called "the exhaustion of susceptibles"

The removal of the pump handle was thus symbolic rather than effective, signalling the beginning of the end of cholera as an epidemic disease in this country That that end was not at once achieved is a sad reflection on the scientific and moral climate of the times For, as a contribution from Prof James Mackintosh reminded the meeting, much of England's prosperity in the reign of Queen Victoria was illusory and its morality superficial The local vestry dealing with the Broad Street epidemic was rebuffed by Sir Benjamin Hall, and for years after the outbreak Lankester, Snow's helper and friend, protested forcibly against the failure to close the surface water pumps in the district Snow's views were attacked in the *Times* by the secretary of the Private Enterprise Association, whose disinterested ness was clearly suspect, but even within the profession his ideas received little encouragement Men of manifest good will, such as Simon, were so overwhelmed by Chadwick's *Report on the Sanitary Condition of the Labouring Population* that they were unable to conceive of a specific agent of disease other than the vague miasmata rising from filthy environment With shame we acknowledge that *The Lancet* accused Snow of riding a scientific hobby-horse by insisting on the paramount dangers of the sewer Despite his solitary abstemious habits and his lack of eloquence, Snow, by the weight of his circumstantial evidence, eventually had his views generally accepted So today we join in honouring the work of a man who rid his country of cholera, not by technical innovation, but by courageous application, acute observation, and an inspired and logical arithmetic

HEAD INJURIES IN AMATEUR BOXING

IT has been estimated[1] that after five years' fighting as many as 60% of professional boxers have detectable mental changes, and that 5% have the slow dementia, rigidity, and tremor of punch drunkenness Less is known about the risk to our 100,000 amateur boxers[2–4], but obviously this is not so great

Electro-encephalographic (E E G) changes in boxers have been extensively studied Dow et al[5] found that such changes tended to disappear thirty minutes after the injury, but Busse and Silverman[6] reported persistent abnormalities in over a third of 24 professional boxers, compared with Gibbs's[7] figure of 15% for controls The degree of E E G abnormality could not be correlated with the length of the boxing career, but the more severe disturbances are found in men who have been knocked out and in the less efficient fighters Larsson and his associates[3] studied 75 amateur boxers, of whom 44 were examined both before and after their bouts and the remaining 31 only because they were suspected of having sustained head injuries An E E G record was taken within thirty minutes of the match In the first group 1 in 8 of apparently uninjured boxers had E.E G abnormalities—a proportion close to that found from records taken before the fights—but after knockdowns or knockouts the abnormality rate rose to about 1 in 2. Of the 31 boxers suspected of having sustained head injuries over half showed E E G abnormalities Control studies excluded effects on the E.E G of physical exertion, and it seems probable that, in the first group, recordings before the fights eliminated confusion due to maturation defects

As Blonstein and Clarke[2] point out, ideally every boxer should undergo E E G examination before taking up boxing By comparison of the initial record with subsequent records the clinical significance of E.E G changes might be made clearer Meanwhile the risks to amateurs of repeated minor cerebral damage cannot be accurately assessed, but it seems most unlikely that these ever lead *to the severe disorders sometimes found in professionals*

MECHANISM OF FEVER

THE body-temperature remains constant by a fine balance between heat production and heat loss Except for slight diurnal variations and the ovulatory rise in women, the temperature in health is remarkably constant. We are almost entirely ignorant of the mechanisms by which the body-temperature is increased in *disease*, the metabolic effects of pyrexia, and whether pyrexia is advantageous to the organism[8]

Some stages in the febrile response have been identified experimentally The administration of a pyrogenic substance is followed by a latent period, varying between species but constant for a given species, in animals it lasts for 15–30 minutes, and in man for 45–90 minutes During this interval there is a leucopenia,[9] owing to sequestration of leucocytes in small blood vessels.[10,11] Wood[12] has suggested that during this sequestration the leucocytes release a pyrogenic substance, which, according to Fair et al,[13] combines with a factor contained in the α or β globulin in the serum It is not known how this factor or other factors exert their effects but they may act directly on the thermoregulating centres

The suppression of pyrexia by cortisone[14] has been studied by Atkins et al,[15] who induced fever in rabbits by administering either pyromen or native dextran They found that such suppression was independent of the initial leucopenia, and the "serum factor" was unaffected They concluded that cortisone must produce its antipyretic effect by acting on some "later and as yet undefined" stage of the fever mechanism

As Atkins et al remark, artificially induced fever may involve mechanisms other than those which operate in man Long[16] has shown that whereas man, monkeys, and guineapigs react similarly to cortisone, rats, mice, and ferrets react differently In evaluating the effects of cortisone, differences between species may be of the utmost importance Finally, it could be equally well argued that cortisone was producing its antipyretic effect in rabbits by interfering with the liberation from leucocytes of the postulated initial pyretic substance

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1 Carroll, E J *Amer J med Sci* 1936 191 706
2 Blonstein J L Clarke, E *Brit med J* 1954 ii 1523
3 Larsson L E, Molin, K A, Nordström Öhrberg, G Silfverskiöld, B P Öhrberg, K *Acta, Psychiat Kbh* 1954 suppl 95
4 Kaplan H A Browder, J *J Amer med Ass* 1954 156 1138
5 Dow R S Ulett G Raaf, J *Amer J Psychiat* 1944 101, 174
6 Busse E W, Silverman, A J *J Amer med Ass* 1952, 149, 1622
7 [illegible] F A Gibbs E L, Lennox W G *Arch Neurol* [illegible]*iat* 1943 50 111
8 Wright, G P Introduction to Pathology London, 1954
9 Römer, F *Berl klin Wschr* 1891, no 36
10 Garrey, W E, Bryan, W R *Physiol Rev* 1935, 15 597
11 Levson, I R. Essex, H E *Amer J Physiol* 1953, 172,
12 Wood, W B *Amer J Med* (in the press)
13 Farr R. S, Clark S L, Proffitt, J G Campbell D H *Am*
J Physiol 1954, 177, 269
14 Recant L, Ott, W H, Frischol, E F *Proc Soc exp B*
N Y 1950 75 261
15 Atkins E, Allison F, Smith, M R. Wood, W B *J exp Med*
1955, 101, 353
16 Long, D A *Lancet* 1954, i, 529

Special Articles

RESEARCH AND THE PATIENT*

L J WITTS
M D Manc., D.M Oxfd F.R C.P
UFFIELD PROFESSOR OF CLINICAL MEDICINE UNIVERSITY OF OXFORD

THE finance for this new unit has come from the free onies, which are the National Health Service's heritance from the endowments of the old voluntary stem endowments whose size reflected not only the ealth of the surrounding community but also its sense f responsibility for the prevention and treatment of isease. The need for local initiative is greater than ever nder the National Health Service where the risk is that nthusiasm may be stifled and everything reduced to one ead level. We remember how in the time of Spain's reatness, Philip II imposed a highly centralised dministration on her and the ardent spirit which had red her local democracies at home and her conquista ores overseas was quenched and died. We remember oo Albert Schweitzer's warning

> "If a comprehensive organisation is established in any epartment of social life the results are at first magnificent ut after a time they fall off. It is the already existing esources which are realised at the start but later on the structive influence of such organisation on what is living nd original is clearly seen in its natural results, and the ore consistently the organisation is enlarged the more trongly its effect is felt in the repression of creative and piritual activity

Those of us who are engaged in medical education and search fear the treason of the clerks who wish to have verything tidy and circumscribed and who forget that he oak sheds ten thousand acorns to produce another ree and the fish spawns a million eggs to maintain the ace of fishes. Research requires a spirit not of prodi ality but of magnificence using that word as it was used y the Greeks who thought that three virtues are ssential if a democracy is to remain great—proper mbition magnificence and greatness of spirit. If we re to have magnificence in our National Health Service e are more likely to get it from local pride than central uthority.

We are opening a unit in which doctors and patients re going to collaborate freely and consciously in the tudy of disease. This unit has been established not by the University which has a duty to advance knowledge nd in Birmingham has signally advanced it but by the Regional Hospital Board which is responsible for the are of the sick. The board's policy and the collaboration to which it will give rise seem to me both enlightened nd significant. As the surgeon in *The Doctor's Dilemma* aid

> "It's always the patient who has to take the chance when n experiment is necessary. And we can find out nothing ithout experiment"

Cooperation between doctor and patient in advancing ur knowledge of medicine has occurred ever since the Hippocratic school of Greek physicians started to study isease objectively. We depend on the patient for the escription of the symptoms and for much of the natural istory of disease. As in other fields of science however, he descriptive method soon exhausts itself and the alue of modern accounts of disease by patients who have uffered from them is literary and inspirational rather than cientific. Hippocratic medicine was scientific in that t endeavoured to predict the course of illness as the astronomer predicts the appearance of a comet and the chemist predicts the effect of dropping a piece of metallic sodium into a bowl of water. But the endeavour of science is to proceed from prediction to control of the future and the collection of data and the construction of hypotheses must be followed by experiments. In medicine this first takes the form of attempting to alter the course of disease by treatment and once we begin to treat patients we are embarked on the troubled sea of human experiment.

Near here at Edgbaston Hall there formerly lived the physician, William Withering who established the treatment of heart-disease with digitalis the active principle of the foxglove, and who was one of the pioneers of clinical research. This was before the establishment of a hospital in Birmingham and Dr Withering used to see poor people at his rooms without a fee, for one or two hours a day. In this way he saw from 2000 to 3000 patients a year and it was mainly from them that he collected the 163 case records which formed the substance of his monograph on digitalis. From his observations on these patients he was able to show that the foxglove was the active agent in the bunch of simples which the old woman of Shropshire had successfully used in patients with heart-disease and he went on to work out in detail the best method of preparing and administering the drug.

In Withering's work the immediate relief of the individual patient was at all times the primary objective of the physician. It is well known however that the advance in morals which, despite setbacks, we consider to be exemplified by the progress of the human race has been characterised by the postponement of immediate satisfactions for ultimate gains which will be larger and as a rule more widely distributed through society. The question now arises how far this concept is applicable to the practice of medicine if it is granted that the aim of medical science is not merely to predict but to control the future. Are there not occasions when the detailed study of the effects of disease and the deliberate reproduction of symptoms may bring rewards far greater than the immediate resort to traditional remedies?

What I have in mind is exemplified by Beaumont's studies on the young French Canadian Alexis St Martin. Alexis had sustained a gunshot wound which left him with a hole in his side through which could be seen the inside of the stomach and the workings of the digestion. Beaumont who had saved Alexis's life after this dreadful accident went on to study the digestive process through this window on her secrets which Nature had so fortuitously provided. Alexis proved a somewhat reluctant subject and Beaumont had to pay him for his pains, indeed he engaged him as his servant. Beaumont's *Experiments and Observations on the Gastric Juice and the Physiology of Digestion* published in 1833 was the foundation of modern knowledge of gastro-enterology.

Or we may think of C H Blackley of Manchester who published an account of his experimental researches on hay fever in 1873. Himself a life long sufferer from hay fever he was the first to show that hay fever is due to pollen. He produced hay fever in himself and other predisposed people by sniffing the dust of blossoms and the pollen of grass and he showed that the application of pollen to a scratch in the skin resulted within a few minutes in severe itching swelling and sometimes even hay fever. The control of malaria as of other tropical fevers has also depended on experiments with volunteers culminating in the brilliant work of Hamilton Fairley and his colleagues in the last war. Millions of lives have been saved and vast tropical territories made accessible to the human race by clinical research and experiment on malaria.

The long journey which has brought mankind from the little bands of food gatherers of the Old Stone Age

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An address given on May 18 at the opening of the metabolic research unit set up by the Birmingham Regional Hospital Board at Little Bromwich Hospital.

whose life Hobbes described as "solitary, poor, nasty, brutish and short," to the great multitudes who dwell in conurbations like the Birmingham region and have an expectation of life of seventy years or more, has only been made possible by science, and science depends on experiment The pestilences which ravaged mankind on this onward march, the Black Death, typhus, small pox, cholera, and yellow fever, are still at the frontiers of civilisation and would lay waste our cities if we relaxed our guard New diseases, physical and mental, have appeared with the strain of civilised life, the change in human nutrition, the hazards of industry and transport, and the ageing of the population The discoveries of the energy of the atom and of the infinite extent of the universe pose medical as well as religious problems The need for experiment is not likely to diminish

The thousands of patients whom William Withering treated at Edgbaston have gone their way, and of their persons and their feelings no other record remains save his monograph on the foxglove The names which are enshrined in the nomenclature of disease are for the most part those of the doctors who wrote and not the patients who suffered Here, happily, a change is occurring A number of the rarer blood groups are called after the people in whom they were first observed—Kell, Duffy, Kidd—and the newly discovered variant of hæmophilia, Christmas disease, was so called not from the date of the original publication but from the name of the first recognised case We may yet live to see the day when it is normal practice for the patient to join with the doctor in the authorship of a publication on experimental work on his illness

There is at present a good deal of uninspired clinical research, research of which we may say, in Lord Macaulay's words, "The inquiry may amuse us but the decision leaves us no wiser" Apart from ethical problems, therefore, it is a good thing that clinical science and human experiment should recently have come under sharp scrutiny There is need to bring together in frank cooperation the people who do the experiments and those who submit to them If only those things are done which can be explained and agreed to by an intelligent patient, clinical research as a whole will greatly gain Not only what is unreasonable but what is jejune and trivial will not be tolerated A voluntary hospital used to mean a hospital in which the doctors gave their services voluntarily, it may come to mean one in which the patients voluntarily coöperate in research It will be necessary to educate the public to promote understanding of the continued need for clinical research, but it is high time the British medical profession paid more attention to the necessity for educating the public in medicine It is no longer possible to preserve medicine as a mystery, even if it was desirable, for we now have a National Health Service and the State is the major supporter of medical research and of the universities Today, therefore, we celebrate not only the active interest of organisations, such as the Regional Hospital Board, in medical research, but also the realisation by members of the community that clinical research is a joint enterprise, consciously undertaken together by physician, scientist, and patient

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BRITISH ASSOCIATION OF PHYSICAL MEDICINE

THE annual meeting of this association was held at St Thomas's Hospital, London, on April 22 and 23

The Department of Physical Medicine

In a discussion on the rôle of the department of physical medicine, Dr W S TEGNER (London) emphasised the fact that physical medicine had been and was still undergoing changes and that fluidity in the composition and organisation of departments should be maintained Space and ease of access were important and many architects still thought in terms of a rigid design incapable of adaptation As regards staff, doctors, physiotherapists, technicians, and, in many cases, nurses worked together, and there might be difficulties in integrating their various activities to secure efficiency This also raised the question of the relationship of the physiotherapy school to the physical medicine department, and Dr Tegner deplored attempts to use students as a form of cheap labour, particularly where this practice had prompted the opening of a school of physiotherapy Beds and doctors in adequate numbers were required by a physical medicine department since attendances and waiting lists continued to grow all over the country

Dr W A FELL (Cambridge) drew attention to the problems peculiar to a physical medicine department outside London and the bigger provincial centres, where over 25% of the patients might come from more than five miles away and some from as far as twenty miles Poor public transport might mean that patients had to spend a whole day away from home or work to have one treatment, and those with even minor complaints sometimes found it impossible to travel the mile or so from home to the nearest point at which public transport was available The only alternative in these cases was to use expensive hospital transport At present it was necessary to treat patients in the central department because only there could be found the requisite medical and technical staff and equipment There was thus an overwhelming case for the provision of properly constituted peripheral clinics Dr Fell emphasised the particular problems of rehabilitation and resettlement in country districts where the only standard of fitness for work was complete fitness He called for a pooling of brains to solve these problems and an effort to educate doctors in what can and cannot be achieved by physical medicine both in diagnosis and treatment

Dr A. T RICHARDSON (London) said that the maintenance of closed physical-medicine departments was indefensible for any reason, since it wasted the time of patients, doctors throughout the hospital, and physiotherapists, and prevented the general practitioner from having direct access to the physical medicine specialist which was against one of the most important principles of the National Health Service It might be argued that the closed system permitted a filtering of patients referred to physical medicine specialists, but surely they were the very people best fitted to reject cases for which there were no indications for treatment in the department A great deal of time could be saved by a sound system of decentralisation whereby a patient could go to the department with a written prescription—e g, from the dermatologist for ultraviolet light therapy, from the chest department for breathing exercises, or from the orthopædic surgeon for postoperative exercises To achieve real efficiency, however, the physical-medicine specialist and the physiotherapy services must be used intelligently, and this in turn depended on the better training of students in this field of medicine Dr Richardson felt that practitioners in other branches of medicine must have a clear idea of the scope of physical medicine, and he restated, as the best working definition of physical medicine, the triad the diagnosis and treatment of the medical disorders of the locomotor system, the treatment of these and other disorders by physiotherapy, and medical rehabilitation It was now considered that the M R C P or its equivalent was essential for the attainment of consultant status in physical medicine in addition to considerable experience in the specialty, which should carry with it possession of the D PHYS MED There was now a sufficient number of fully qualified registrars to ensure that future consultant appointments would fulfil these criteria

Dr F S COOKSEY (London) expressed his concern at e shortage of physiotherapists, a shortage reflected in her fields such as nursing and school teaching Unless lowering of the standards of training for physiotherapists was to be accepted (a suggestion firmly jected by many later speakers) there would have to be continual economy in the prescription of treatment r Cooksey made a plea for a firm integration of the edicine practised in the physical medicine department ith other hospital services and with the local-authority rvices and general practitioners

Dr C J S O MALLEY (Watford) stressed the impor nce of the remedial gymnast in the rehabilitation team doctor physiotherapist occupational therapist and ualified social worker Dr B W WINDLE (Brighton) ated that mobile centres did not go far to meet the need the peripheral centres in the provinces envisaged by r Fell for the number of patients that could be treated as so small He and other speakers mentioned the pparent ignorance of many members of the profession nd lay committees of the proper function of the qualified hysical medicine specialist and his department Dr RANCIS BACH (London) suggested that joint consulta on clinics with the neurologist orthopædic surgeon and natrician went a long way to solve some of the prob ms involved in the efficient decentralisation of open hysical medicine departments

Hydrocortisone by Local Injection

Dr J H CYRIAX (London) drew attention to the great portance of accurate anatomical localisation of soft sue lesions for the effective use of hydrocortisone and discussed the diagnostic principles concerned

Dr P HUME KENDALL (London) discussing the results btained at Guy's Hospital said that in selected cases of heumatoid arthritis it had been confirmed that the ormone s chief value appeared to be the production of emission sufficient to permit more active physiotherapy han would previously have been possible In osteo rthritis hydrocortisone had been of use only in the early ase or where symptoms had been aggravated by recent njury In acute rotator cuff lesions of the shoulder esults had been good but the effect on the frozen houlder' was usually disappointing Various soft ssue lesions such as tennis and golfer s elbow plantar sciitis, De Quervain s syndrome and tenosynovitis had esponded well In acute traumatic articular effusions ncomplicated by serious bone or ligamentous injury he results were often dramatic even in the presence of hæmarthrosis, where hyaluronidase was combined with ydrocortisone after aspiration

Other speakers described the economic importance of ydrocortisone in terms of time saved by patients and hysiotherapists alike but they suggested that the neces ary associated methods of rehabilitation should not be rgotten

The programme included three short films. Dr Bach intro uced one called *Grip on the Nation* which had been made for he British Rheumatism Association for exhibition to the ublic and was concerned with the prevention and treat ent of rheumatism. Treatment at hospital spa and eripheral clinics, as well as at home was briefly yet clearly utlined

The second film *Neuromuscular Transmission in Myasthenia ravis* was introduced by Dr Richardson and had been made colour for presentation at the American Congress on yasthenia An animated cartoon was used to demonstrate hat happened at the neuromuscular junction during different pes of block

Infantile Cerebral Palsy introduced by Dr W F DUNHAM ondon) consisted of parts of three separate films, the result work done by Dr Dunham in conjunction with Mrs. Elaine ollis, and it demonstrated normal and abnormal reflexes in ildren

GENERAL MEDICAL COUNCIL

IN a presidential address at the opening of the council s 190th *session on May 24 Sir David Campbell referred* to the use in the *British Pharmacopœia* of the apothecaries system of measurement The Pharmacopœia Commission had recommended that a definite decision should now be taken to discontinue the use of the apothecaries system in the *British Pharmacopœia* of 1963

Nearly two and a half years had passed since it had become compulsory for every newly qualified man and woman to serve for twelve months as a house-officer before full registration Similar requirements had already been in existence in South Africa and most of the provinces of Canada while in New Zealand the introduction of such arrangements was synchronised with our own Since that time provision had also been made in Hong Kong Singapore and Malaya for the introduction of corre sponding requirements with effect from Jan 1 *1953* A start had now been made in introducing similar arrangements in Australia In New South Wales the requirements had been brought into effect as from November 1954 This would of course mean that practitioners from this country who wished to practise in New South Wales would be asked to produce evidence of their experience before they could be registered there The New South Wales authorities would not require such evidence of practitioners who were fully registered here before Nov 10 1954.

The means provided by the Medical Acts to enable the Register to be kept correct were simple but somewhat drastic The Acts authorised the registrars to write to any registered medical practitioner at his registered address to inquire whether he had ceased to practise or had changed his residence If no answer was returned to this letter within six months, it became lawful to erase the name of the practitioner from the Register Since 1951 letters had been sent to approximately 50 000 practitioners 2059 were untraced and their names were eventually erased In the past four years 309 names erased in this way had been restored to the Register The President invited each member of the profession to ensure that the registered address was correct and afforded a trustworthy means of communication with him

During the session the council would be discussing the medical curriculum Possibly the council s recom mendations had acquired the force of regulations and had thus come to have a restrictive effect on the diversity freedom and responsibilities of universities and medical schools The President hoped that the council would consider appointing a curriculum committee to consider the whole matter

CENTRAL HEALTH SERVICES COUNCIL

THE Minister of Health has appointed or reappointed the following doctors to the council and standing advisory committees for the period ending March 31 1958

Central Health Services Council

* Sir Stanford Cade Sir Henry Cohen Prof A J Lewis W P H Sheldon * S Wand

Standing Advisory Committees

Medical—* Sir Stanford Cade Sir Henry Cohen Prof A J Lewis H M C Macaulay W P H Sheldon * Stanley Thomas, S Wand

Dental—Prof M A Rushton Prof. F C Wilkinson

Pharmaceutical—P J Gibbons.

Ophthalmic—Macdonald Critchley O G Morgan

Maternity and Midwifery—* Prof W C W Nixon

Mental Health—N H M Burke * T M Cuthbert Prof A. J Lewis, * C A H Watts (until March 31 1956) Denis Williams; one vacancy

Tuberculosis—P M D Arcy Hart Peter Kerley one vacancy

Cancer and Radiotherapy—Sir Stanford Cade Sir Ernest Rock Carling Sir Henry Cohen Sir Charles Dodds F.R.S. Prof J S Mitchell F.R.S., V E Negus Sir Clement Price Thomas (until March 31 1957)

* New member

Public Health

AN OUTBREAK OF LEAD POISONING IN THE CANKLOW DISTRICT OF ROTHERHAM

J A Gillet
M B Lpool D P.H
MEDICAL OFFICER OF HEALTH FOR ROTHERHAM

Late on Monday afternoon, Dec 20, 1954, I had a telephone call from the Children's Hospital, Sheffield, saying that twin boys Keith (case 1) and Kenneth (case 2) B - y, aged 3½ years, had been admitted earlier that day and that a diagnosis of lead encephalopathy had been confirmed It was also stated that a younger brother James (death B), aged 2 years, had died on Dec 15 in the Doncaster Gate Hospital, Rotherham, having had symptoms like those from which the twins were suffering After a post-mortem examination his death had been attributed to status epilepticus due to idiopathic epilepsy

The general practitioner, who had diagnosed lead encephalopathy, informed me that case 2 had been admitted to Moorgate General Hospital, Rotherham, on Dec 12, but had been discharged home on Dec 14, at the parents' request, and had later been admitted to Sheffield Children's Hospital with his twin brother (case 1)

ACTION TAKEN

Next morning I visited the home of the children, together with the Chief Sanitary Inspector and the Area Health Visitor, but, as the mother was out, we visited the home of the grandmother, from which the twins were admitted, and where they had spent a good deal of their time

The grandmother was edentulous, anæmic, and constipated and complained of a metallic taste in her mouth (subsequent investigation showed no stippled cells or signs of lead poisoning) An adult son and a younger married daughter and her baby were also examined The daughter and her baby appeared healthy, but the son had a suspicious-looking blue line on his gums (subsequent investigation in his case also proved negative)

A thorough investigation of the house yielded no evidence of the source of lead, there was no fresh or damaged paintwork, there were no lead toys, and a recent routine analysis of the water-supply showed that it was free from lead Inquiry, however, elicited the fact that for some time car battery casings had been used as fuel for the domestic fire and a sample was taken from the ashes in the hearth and a piece of battery casing from the coal-house These battery casings seemed to be the only source of lead which could have caused the poisoning

The Area Health Visitor provided the information that it was a fairly common practice in that district of the town to burn battery casings as domestic fuel, and it was decided that immediate action must be taken to warn people of the danger of this practice Arrangements were made for the police loudspeaker van to tour the area and broadcast the following message

> Do not burn any more car batteries—they are dangerous and can poison you

All local newspapers were contacted and a short statement was given setting out the facts

The Chief Sanitary Inspector organised a house-to-house visit of the affected area by the sanitary inspectors, and the collection of names, ages, and addresses of all people living in houses where they admitted to burning the cases The main source of supply—a scrap metal dealer—was traced and the supply was stopped

Meanwhile, the Pædiatrician attached to the two Rotherham hospitals had been contacted, and from him it was learned that about a month before, on Nov 21, Leonard B h (death A), aged 5 years, had died, the cause of death, following a post mortem examination, being given as cholæmia and infective hepatitis This child's history was interesting in that he was closely related to the twins and their brother (cases 1 and 2 and death B) It seemed likely that he had in fact died from lead poisoning

At the same time the Rotherham Pædiatrician informed me that Leonard's two brothers Roy (case 4), aged 20 months, and Alan (case 5), aged 7 years, had attended the outpatient department, and I was asked to get them up to hospital urgently for investigation because, in the light of events, it was felt that their symptoms were suspicious This investigation confirmed a diagnosis of lead poisoning, and they were admitted to Moorgate General Hospital the same day (Tuesday, Dec 21) being transferred two days later to the Sheffield Children's Hospital. Later that day I was informed that a further child, Franc B w (case 3), aged 20 months, had been admitted from the same district in Rotherham to the Sheffield Children's Hospital with suspicious symptoms

On Dec 23, Ruth B - y (case 6), aged 5 years, who was sister to cases 1 and 2 and death B, was admitted to Sheffield Children's Hospital, and on Dec 24 two further cases, Kenneth P (case 7), aged 7 (a mental defective), and Kenneth S (case 8), aged 20 months, were admitted from the same district of Rotherham as the other [illegible] cases

By the evening of Tuesday, Dec 21, as children appeared to be at greater risk than adults because of the danger of encephalopathy, it was felt that efforts must be concentrated primarily on them Arrangements were therefore made with the Pathologist at Moorgate General Hospital that a shuttle service of ambulances and cars would be run between the homes and the laboratory on Thursday, Dec 23, so that all known child contacts could have a blood film and blood-count, and any doubtful cases could be referred to the Pædiatrician

By the evening of Dec 21 the survey by the sanitary inspectors had produced the information that 70 children and between 40 and 50 adults from 22 houses had been involved. As it was suspected that householders were not admitting to exposure, the press were asked to publish a warning about the seriousness of lead absorption with delayed symptoms in children This produced an increase in numbers so that by Wednesday night, Dec 22, 127 children and 123 adults from 40 houses were found to have been at risk

During Wednesday households were visited and all battery casings surrendered—together with ash, which it was felt constituted an important hazard—were transported and disposed of by a Health Department van Over three tons was collected in this way

During Wednesday, householders were informed of the arrangements for examining the children the next day and also that Health Department medical officers, accompanied by health visitors, would visit each suspected home that evening and examine the adults for clinical signs, which would decide whether a blood examination was necessary for them The medical officers were given lists of names and addresses and asked to complete the following form for each case seen

Suspected Lead Poisoning

Full name ——————————— Age —
Address ———————————————
Name of family doctor ———————————
For about how long have batteries been burned in the house? ———————————
Condition of gums and teeth (if any) ? blue line
? Anæmia ———————————
Any other symptoms (e g, anorexia constipation habits wrist drop foot drop) ———————
? Blood test required ———————————
Any other comments ———————————
Signature of Medical Officer ——————— Date —

On Wednesday the following circular was sent out by hand to all general practitioners in the area

"As you may be aware cases of lead poisoning have occurred in the Canklow district of Rotherham The cause has apparently been the burning on domestic fires of old motor car batteries. So far approximately 60 children in the area are thought to have been at risk and arrangements are being made for these to have a blood test (to examine for stippling) at Moorgate General Hospital Laboratory X ray examinations of bones may be required later depending upon the result of the blood test These procedures are necessary on account of the potential seriousness of the condition in children and the possibility of lead encephalopathy Should you become aware of any cases in your practice I should be glad to be informed. In adults the condition may not be so serious but arrangements are in hand for homes in which the batteries have been burned to be visited by members of my staff Adults showing a blue line anæmia or other suspicious symptoms will be referred for blood examination. Should I become aware of an established case of lead poisoning in your practice I will notify you as soon as possible

The Physician Superintendent of the Moorgate General Hospital was contacted on Wednesday Dec 22 with a view to making arrangements for the medical examination of suspected cases among the adults and he agreed to hold a special outpatient session if necessary for this purpose At the same time he agreed to admit to hospital immediately any cases of lead poisoning that the general practitioners felt should be admitted

During the evening of Dec 22 127 adults and children were examined in their homes by medical officers of the Health Department accompanied by health visitors and all children and all doubtful adults were referred to the Pathological Laboratory at the hospital for blood test.

During the morning and afternoon of Thursday, Dec 23 a shuttle service of ambulances and cars conveyed children and a few adults, to the laboratory escorted by health visitors Subsequently parents and children attended the laboratory unaccompanied either because of advice given by the health visitors sanitary inspectors or their own doctors, or because they had heard that their blood could be examined and they wished to be reassured that they were in no danger after being exposed to risk

The health visitors later assisted in the persuasion of defaulting members of families to attend for tests The Sanitary Inspectors continued their house to house visits and by Dec 31 had paid 1039 visits to houses

As more cases came to light a number were found to be affected by jaundice and investigations were made into the possibility of this being caused by some toxic substance present in the battery casings Antimony seemed to be the only substance of this type which was present and it was felt that the amount present was not sufficient to produce jaundice

I am satisfied that the jaundice was in fact infective jaundice partly because there were several minor epidemics in the Canklow district of Rotherham and in areas around Rotherham and partly because a sister who attended one of the first cases of encephalopathy to develop jaundice became jaundiced herself four weeks later In some cases the jaundice was responsible for producing symptoms of acute lead poisoning in children already suffering from lead absorption or chronic poisoning

By Dec 31 287 blood specimens had been taken and 240 of these had been analysed and by Jan 7 330 had been taken and examined A further 14 bloods were taken and analysed during the following week making a total of 344

Of these 122 were from adults and 222 from children and infants These were apart from the 8 children who had been admitted to Sheffield Children's Hospital 3 of whom were transferred there from Moorgate Hospital Rotherham, in order that they might have the advantage of treatment by calcium disodium versenate which was available there

Of the 122 adults 55 with suspicious signs such as anæmia were referred for clinical examination by the Physician-Superintendent of Moorgate General Hospital Only 27 of these could be persuaded to attend in spite of repeated requests and in spite of arrangements being made to hold clinics at special times convenient to them

Of the 222 children and infants 112 were referred to the Rotherham Pædiatrician for further investigation

No cases of lead poisoning have been diagnosed in adults

124 reports have been received so far on the infants and children This includes a number of children who were already attending the hospital but were called up for special review in the light of events

	Lead poisoning	Lead absorption	Negative
Inpatients	5	13	4
Outpatients	0	36	66
Total	5	49	70

All inpatients have been discharged from both hospitals The last to be discharged were cases 1 and 2 who were discharged on Feb 23 to the care of their own doctor

On Saturday Jan 8 James B y (death B), aged 2 years and Leonard B h (death A) aged 5 years were exhumed on the instructions of the Rotherham Coroner and a post mortem was performed Analysis of the organs indicated that these two children had died from inhalation of lead and at the adjourned inquest on Feb 10 the jury found accordingly, adding a recommendation that steps should be taken to prevent the burning of car battery casings

FOLLOW UP

Arrangements have been made for those cases where it is recommended by the pædiatricians and where it is felt that the parents cannot afford this that a pint of free milk is supplied daily Payment for this will be made from a voluntary fund which is at my disposal In the first instance the supply is given for a month and will be extended if necessary to meet clinical requirements The pædiatricians will continue to follow up the cases clinically but in view of the possibility of mental retardation following lead poisoning in children which has been reported by some authors it is proposed that certifying school medical officers shall conduct intelligence tests on all children diagnosed as having suffered from plumbism All tests which are made will be repeated in approximately six months time and again after a year Four of the children have already been tested in this way and the intelligence quotients (Terman and Merrill form L) are 81 73 83 and 91 The two original cases have been seen by a psychologist attached to Sheffield University Education Department and he gives the intelligence quotient (Terman and Merrill) as 72 for Keith and 63 for Kenneth

THE BATTERY CASINGS

The battery casings vary slightly in composition as between the products of one firm and another, but in the main they are made of vulcanite which is composed of a mixture of bitumen asbestos and ebonite

The essential unit of the battery is the plate containing a conductive framework or grid which holds the active lead material It is made of lead 88-93% antimony 7-12% and tin 0 3 0 4% with small quantities of arsenic and copper (0 05% in total)

The grids for the positive and negative plates are of similar construction The paste most commonly used as a filler for the grids consists of litharge (PbO) or red lead (Pb_3O_4)

or a mixture of the two The mixture is made into a stiff paste with sulphuric acid when a reaction occurs which leads to the binding together of the material on account of the formation of lead sulphate and peroxide (PbO_2) These plates after drying are alternately oxidised and reduced by electrolysis in dilute sulphuric acid The final result is that the paste of the negative plates becomes reduced to metallic lead and that of the positive oxidised to lead peroxide

Accumulators in repose contain, besides small quantities of litharge and red lead, three active substances—spongy lead on the negative plates, spongy lead peroxide on the positive plates, and dilute sulphuric acid between them. Sulphate of lead is formed on both plates during discharge and brought back to lead or lead peroxide during charge The separators between the plates are made of porous wood, or more recently of porous rubber or plastic

During use, and especially when the life of the battery is nearing its end, small particles of the various constituents of the plates including some metallic lead, lead peroxide, and lead sulphate become detached and fall to the bottom of the casing where special recesses are constructed below the plates to receive these particles so that they shall not interfere with the conductivity of the battery In time a slimy grey brown deposit of these constituents is formed which consists largely of lead sulphate

The old batteries are purchased from various sources such as Government sales, and from firms who run a part-exchange system replacing the old battery by a new one and making a small cash adjustment They are brought to the scrap yard and dumped ready for breaking up In the particular scrap-yard involved, in the present investigation a sledge hammer is used to crack the casing, the sulphuric acid is allowed to run out, and the lead plates are salvaged while the broken casing is treated as waste, being placed on a dump where members of the public came to buy or otherwise acquire them, taking them home in sacks, in wheelbarrows, or in some cases in the family perambulator There they were stored in the coalhouse or in the open until they were burnt on the fire

Many of them had been put to a variety of uses In some cases the children were allowed to use them as bricks for play, in others they had been used as ladles for conveying pig food to the trough, and they had also been burnt on bonfires both in the open and in one case in an air raid shelter

RESULTS OF BURNING

The casings burn well but with a very smoky flame and an obnoxious smell, and small hot fragments tend to become detached and to be projected from the fire into the room Several children seen had sustained small burns on exposed arms and legs from this cause

An attempt was made by the Chief Sanitary Inspector to reconstruct the circumstances in an empty council house of a similar type to the houses on the estate involved A fire was lit and car batteries were burnt throughout the day and the following analyses were made by the Sheffield Public Analyst

(1) Deposit removed from portion of battery case expressed as lead sulphate	82 %
(2) Dust and fragments from breaking up of battery cases expressed as lead sulphate	10 46 %
(3) Cinders from burning of battery cases expressed as lead sulphate	1 5 %
(4) Flue dust	12 50 %
(5) Hand washing water	0 024 %

A sample of flue gas and air in the room used for the experiment failed to reveal the presence of lead

A further test using a closed stove has been made and in samples of flue gas taken no lead fume could be detected

The temperature of the stove fire was recorded during this experiment varying between 700°C and 1000°C An unofficial report has been received from an industrial firm (not in Rotherham) who have for some years made a practice of burn battery casings on a furnace This indicates that repeated tests of flue gases have failed to reveal lead fum and that the tendency is for any lead present to melt and to fall through the bars of the furnace

These results show that considerable quantities of lead and lead salts were involved, and that very little if any of the lead salts or of lead fume escaped by the chimney In fact the temperature of an ordinary domestic fire would not be sufficiently high to produce "fuming" of the lead

The chemical changes produced by burning would depend on the temperatures reached Margaret Fishenden in her book *House Heating* quotes Darling as giving the average temperature of a brightly burning coal fire at about 1407°F (764°C) She also states that the radiating surface temperature will generally be above 1000°F (538°C) and below 2000°F (1093°C) and later on gives limits of 750°F (398°C) to 1750°F (954°C) with a mean of 1500°F (827°C) For purposes of convenience it can safely be assumed that the temperature of a domestic coal fire does not exceed 1000°C

The following pertinent figures are given in *Lange Handbook of Chemistry* (1946)

Lead

Melting point	327°C
Boiling point	1620°C

Vapour pressure in mm mercury	
808°C	0 08 mm
996°C	1 75 mm
1178°C	10 80 mm
1620°C	760 00 mm.

Other lead compounds

	Melting point
Lead sulphate	1170°C
Litharge (PbO)	888°C
Lead peroxide (PbO_2)	290°C (with decomposition)
Red lead (Pb_3O_4)	500°C (with decomposition)

Assuming a temperature of 1000°C as being that of a domestic fire, the chemical changes taking place are

(1) Red lead and lead peroxide break down to produce litharge

(2) Litharge is reduced to produce metallic lead

(3) Lead sulphate is unchanged.

(4) Metallic lead produces very little fume at that temperature and the small quantity which was produced would be carried up the chimney by draught The distance it would travel would be very short as it would rapidly cool and it would be precipitated in the flue or fall back into a fire grate

These facts rule out the possibility of poisoning, by inhalation of lead fume and explain the results of chemical analysis obtained and in particular

(1) The failure to detect lead in the flue gases

(2) The presence of lead in the flue dust

THE ASH

Two possible sources of lead are left

(1) In the fresh casings

(2) In the ash

There are also two possible portals of entry

(1) By ingestion—due to contamination of fingers and foo or in the case of smaller children by sucking pieces of batter casing

(2) By inhalation of ash

The post mortem findings in the two children who di showed

Death A	Lungs 0 24 mg	lead per 100 g tissue
	Liver 1 12 mg	" "
	Kidneys 1 39 mg	" "
Death B	Lungs 0 29 mg	" "
	Liver 1 28 mg	" "
	Kidneys 1 56 mg	" "

The fact that in death A the liver contained almost f times as much lead as the lungs and less than the kidn and in death B the liver contained almost four times much lead as the lungs and less than the kidneys stated to indicate that the poisoning was due to tion as a case of lead poisoning by mouth was quoted where the liver lead was thirty times the lung lead and more than the kidney lead But this conclusion, which was based on the findings in one case only did not take into account that both children were jaundiced for some time before death—death A severely and death B slightly This would tend to interfere with the absorption of lead taken by mouth

Although the route of entry of lead into the system must remain a matter of conjecture it is interesting to study the ages of the affected patients In 293 adults (i.e., over the age of 15 years) at risk only 1 case of lead absorption was detected and this was in a girl of 15 In the 232 children under the age of 15 at risk it is a striking fact that of a total of 55 cases of lead absorption or lead poisoning 51 were under the age of 7—i e of an age where they are likely to put things in their mouths The youngest child affected was 10 weeks old lived in a household where the standard of hygiene was not good, and is the proud owner of a dummy which is not an unlikely vehicle for conveying lead contaminated ash from the floor to his mouth

PROTECTION OF THE PUBLIC

In the outbreak under investigation the wide publicity which was given locally to the dangers associated with the burning of battery cases and the weight of local public opinion were sufficient to cause the cessation of this practice and to prevent the scrap dealer concerned from allowing the public to have access to the casings But it is a striking fact that the dealer informed me that some two weeks after the initial cases had been discovered, and while the publicity given to them and to others was at its height he was approached by several people who asked for casings to be used as fuel. He refused to supply them.

It is another striking fact that in one family where at least three of the children were known to be affected though without any gross symptoms, and where the mother herself showed some signs suggestive of lead absorption, the parents complained that a source of cheap fuel had been closed to them stating that they were prepared to continue the practice of using them as fuel and were only discouraged by the opinions of their neighbours and by the fact that no casings were available

So far as I can ascertain there is no law to prevent the scrap-dealers from disposing of this waste material as they wish, or from dumping it in such a place that the public have free access to it It is extremely doubtful whether any action could be taken by an aggrieved person against the supplier of the battery cases, even though he might be aware of the potential danger attached to them Nor do there appear to be any powers to prevent people from using the material as domestic fuel unless one could make use of section 92 of the Public Health Act 1936 which is very dubious.

Failing this it might conceivably be possible if there were children in the home to make use of section 1 of the Children and Young Persons Act, 1933 on the grounds of neglect—though the successful outcome of a prosecution under this section of the Act would also be very doubtful and in any case could only be considered after the damage to the child had already occurred and the practice was continuing

It appears that provision should be made for the registration and inspection of premises used for this purpose as well as for the safe disposal of waste

Undoubtedly the safest method of disposal would be controlled tipping and burying of the material If incineration in a destructor is to be the method of disposal cleansing of the battery casings by hosing should precede burning in the destructor to remove as much of the adherent lead salts as possible This procedure would no doubt leave a certain amount of lead salts in the cracks in the casings; but, even though the forced draught of the destructor might convey some of the dried lead salts up the chimney it is doubtful whether, providing the casings were diluted with other waste materials during burning there would be any appreciable pollution of the atmosphere

Poliomyelitis Vaccination

The number of children in the United States who have had poliomyelitis shortly after vaccination stood at 79 on May 21 [1] There have also been about 30 reported cases among people in close contact with vaccinated children who did not themselves have any illness.[2] The significance of this new development is hard to judge without more details of the present incidence of all forms of poliomyelitis in the United States, but the total of contact cases seems too large to be explained by natural infections and it is difficult to avoid the conclusion that the vaccination was in some way involved And, as we observed earlier,[3] the most likely cause is incomplete inactivation of virus in certain batches of vaccine

The future course of the vaccination programme in the United States was to be discussed at a meeting in Washington on May 23 It has been suggested that the decision may be to postpone further vaccinations until the autumn At present the clearance of vaccine has been stopped to await the results of a re-examination of manufacturing methods and safety tests. But children are still being vaccinated with previously cleared vaccine, and in New York on May 20 22 827 school-children had their first injection [4] This figure was 69% of the expected number judging from the total of parents who had originally agreed to vaccination. On the day before when New York's programme began 71 5% of the expected number had been vaccinated

The poliomyelitis advisory committee of the United States Public Health Service have been considering among other things the possibility of using smaller doses of vaccine given subcutaneously and they set out their recommendations in a statement published on May 20 [4] They believe that it would be unwise to recommend procedures which are less effective antigenically, and they recommend sticking to the three intramuscular injections of 1 ml. The second dose should be given two to six weeks after the first, and if possible before the poliomyelitis season begins although the second dose is beneficial even if given after a number of months" The third dose should be given about seven months after the first. This, the committee say, produces the best antibody response They add that, in their view, the administration of vaccine during an outbreak of poliomyelitis has its place in preventive medicine The second dose can be given during an outbreak without appreciable concern for the phenomenon of provocation since slight immunity resulting from the first dose of vaccine will most likely provide protection against any such effect.

Marriage Statistics

The Registrar General has lately published part II (the civil tables volume) of his review for 1953 [5] Among the less familiar indexes of human welfare is the marriage-rate which in 1953 was 15·6 persons married per 1000 population in England and Wales There were more marriages in the London and South Eastern Region than elsewhere—the rate being 16 7 The most popular months for marriage were March and August and the least popular November The most common age for marriage remained 2? for men and 21 for women and there was more intermarriage between men of 23 and women of 21 than between men and women of any other combination of ages

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[1] New York Times May 21 195

[2] Manchester Guardian May 23 1955.

[3] Lancet May 7 1955 i 9.6

[4] New York Times May 21 19 5

[5] The Registrar-General's Statistical Review of England and Wales 1953 Part II Civil. H.M. Stationery Office 1 p 174 4s

In England Now

A Running Commentary by Peripatetic Correspondents

WHEN you take your child to the follow-up clinic the doctor says, "Well, Mrs X, and how is little Johnny's nose (or throat, or chest) now?" And you say, "Much better, doctor He's a different child since his operation" Whereupon Doctor, Sister, and you all beam at one another and at little Johnny, and a hieroglyphic on little Johnny's case sheet adds to the statistically significant successes in nose (or throat, or chest) operations

But supposing some of the Mrs Xs said some of the things left unsaid? It is perfectly true that the little Johnnies are different children since they left hospital, but if their mothers described in detail some of the differences the interview would be something like this

Mrs X "Well, Doctor, his nose (or throat, or chest) is certainly better, but he's *a different child since his operation* He's so fussy over his food now—won't eat anything with a spoon any more, just biscuits and bananas, and he used to be so good over his dinners He won't use the pot any more, Doctor, he always does it on the hearthrug now He won't go out to play alone It's 'Mummy, Mummy, where are you?' all day long And he's dreadful at night—scenes over going to bed, and he wakes up screaming with dreadful dreams about blue ladies"

This is all rather near the bone for us, as our under-3 has just spent twelve days in hospital (Excuse me while I go and sponge the hearthrug) He takes a very long time over his meals now, though he used to be the world's fastest eater, but he does get it all down eventually, and he's already back to his preoperation weight He's developed a siren scream when thwarted, so high-pitched that if only it was a little higher I should be spared from hearing it At bed-time he calls out again and again, and begs me to sit on his bed and hold his hand He keeps asking for drinks—anything, in fact, to postpone going to sleep It's usually his brother (over-5) who calms him down I hear him shouting in great irritation, "*Do* shut up! I can't hear myself sing"

Over-5 feels that too much fuss has been made of under-3, and though we try to avoid mentioning hospitals, injections, and so forth, over-5 has no such fine feelings. He opened the door to our kind and charming surgeon and at once said, "Here's Mr B come to take you back to hospital!" When I remonstrated with him (after the ensuing hubbub had died down) over-5 said, with elder-brotherly candour, "Well, I hoped he was!"

* * *

The visitor to the Principality may think that such appellations as Thomas-the-Fish, Harries-the-Hearse, or Dai-small-coal are applied frivolously But the natives are in earnest when they attempt to compensate for their ancestors' lack of imagination in the matter of surnames The flexibility and scope of the system were shown by my Welsh patient lately

After responding rapidly to my treatment of his pneumonia, he was unfortunate enough to prolapse his lowest gut, and I paid him social visits in the surgical wards Later, while I was away, he came again to the hospital, this time as a visitor to his small son, recovering from a tonsillectomy Wishing to be remembered to me, but realising that even in London his surname was about as common as the cases of fog pneumonia, he pondered some way of identifying himself Wales came to his aid "*Please tell Dr D,*" he said to the house-surgeon, "that very best wishes are sent by Evans-the-Rectum"

* * *

Driving has always been a bone of contention in our family, and I have never been allowed to forget that I failed my first driving test at the age of 17, whereas my wife passed hers, first attempt, at the same age So it was with considerable trepidation that I approached my test in the States "Well, brother," said the examiner, as he moved his gum from one corner of his mouth to the other, and brushed aside my British licence, "what is a soft shoulder?" Resisting an impulse to be facetious, I told him, for I had studied the book as intensively as if I were preparing for the membership When he had visual fields and colour vision and we had spent some ten minutes discussing the technicalities of right-of way at intersections and school bus laws, we sauntered out to the roadway Just then a little A 30 went bowling past along the road "Gee," said the examiner, "just look at that cute little English car O K in your country I guess, but not over here, no protection!" As I digested the significance of his remarks and let in the clutch, I heard him say "They tell me they drive on the left in your country" I murmured assent "Is that so," he drawled, shaking his head over this curious idea My memory of the succeeding half-hour is dim, but I know that in the heavy traffic and unfamiliar surroundings, it was a harrowing experience as we performed every conceivable manœuvre. As I clutched my newly won licence, my account at home that evening, though lurid, was given with an air of conscious superiority When my wife's turn came a few days later, she was trembling visibly As she went to face the inquisition I settled down in the car prepared for a long wait. But only a few seconds had elapsed when she and the examiner returned to the car; in a few moments more she had driven 50 yards down the road and back and her test was over We drove home in silence The demands for equal pay for women leave me cold, coming from a sex which enjoys so many other advantages

* * *

It may or may not interest the Royal College of Physicians to know how high it stands in my bank manager's estimation His branch is small enough for him to take a personal interest in the details of his clients' accounts He tends to judge one's social stature by the club to which one belongs, and the standing of the club by the size of its subscription I am high on his list, for he has long regarded the college as among the more exclusive of the Pall Mall clubs, my regular half-yearly 15-guinea "subscription" has fostered and maintained this illusion But now even the Athenæum pales into insignificance since the clearing-house informed him of my latest contribution—for more than twice the usual amount.

It will be six months before he suspects what my pride forbids me to explain to him, that there will be no more "subscriptions" At last I have passed the membership.

* * *

I have been less fortunate than my peripatetic colleague who finds "Lie down on the couch, please" an adequate instruction The keen patient asks which way up, and blow me down, even then he may get it wrong When I want to examine the back as well as the front I specify the position, but accept whichever is adopted without comment, except "Now turn over" at the appropriate stage There is, however, still the rara avis who suddenly realises he is wrong and turns over with profuse apologies in mid-palpation Against him I know of no defence except patience

* * *

It was just before a previous general election, I remember, and the patient was in a tragic state of almost complete quadriplegia due to the most severe subacute combined degeneration of the cord that I have ever seen Though he had a large intractable bed-sore, he kept up his morale well, but he could not quite stand up to the political arguments of the other patients A staunch Conservative in the past, he was fast succumbing to the ward influences and beginning to wonder whether he ought to vote Labour this time

We thought we might be able to stimulate the indolent tissues of his bed-sore by daily doses of testosterone. The effects were pronounced but unforeseen The bed sore remained much as before, but his morale and strength of will improved so much that he was now able to argue back with vigour in the ward political discussions To such effect did he do this that he actually converted several of his fellow patients to the Conservative point of view Perhaps there is a future for political endocrinology in influencing the floating vote

* * *

I was so stirred by Dr Cicely Williams's hexameters in last week's *Lancet* (p 1071) that I should like to offer this tribute to her learning *utriusque linguæ*

MACTA PUELLA VIRTUTE NOVA

Cæciliæ jam cede locum, sermone Latino
Quæ Kwashiorkorem vindicat ipsa suum

Letters to the Editor

THE MYSTERY OF DENTAL CARIES

SIR,—With regard to your leader of May 14 I venture to suggest that the "mystery" has been overstated. It has been shown that the exciting factor in the production of dental caries is the achievement of a high sugar concentration on the tooth surface and maintenance of this condition for comparatively long periods of time. This is associated with two factors: the frequency with which the sugars are taken into the mouth and the physical nature of the sugars. Exhaustive investigations into dental caries carried out under the auspices of the Royal Medical Board of Sweden first published in 1952 reached the following conclusions:

(1) The consumption of sugar can increase caries activity.

(2) The risk of sugar increasing caries activity is great if the sugar is consumed in a form with a strong tendency to be retained about the teeth.

(3) The risk of sugar increasing caries activity is greatest if sugar of that form is consumed between meals, thus increasing the number of times a day that sugar is taken.

These findings have been endorsed by many other investigations.

In the M.R.C. investigation both control and experimental groups received sugar with meals. Their oral sugar clearance time was probably similar, and it is therefore no surprise that the dental caries was also similar in the two groups.

Eastman Dental Hospital
London W.C.1

G. J. PARFITT

MESTINON IN MYASTHENIA GRAVIS

SIR,—'Mestinon'[1] (pyridostigmine bromide) is the dimethyl carbamate of 3 hydroxy 1 methyl pyridinium bromide, an analogue of neostigmine. It is said to be longer acting and less toxic than neostigmine.

The clinical value of this drug has been assessed in 10 cases of myasthenia gravis. During this trial one tablet (15 mg.) of neostigmine was taken to be equivalent to one tablet (60 mg.) of mestinon.

Of these 10 patients, 7 expressed a preference for the new drug because they felt its effect was greater and lasted longer than that of neostigmine; 1 found no difference; and 2 preferred neostigmine on the ground that the side-effect of abdominal discomfort was accentuated by mestinon. In this respect the other 8 patients found this symptom, if anything, less troublesome.

Allowing for the natural reaction of most of these patients to interpret any new form of therapy as being better than their present one, the best assessment of the usefulness of the drug can probably be gained from a study of the disease in its severest state. 2 of our patients were in this condition. Both required large doses of neostigmine every two hours during the day and had to be roused for further doses every three hours during the night. Despite this heavy dosage they were extremely weak on rising in the morning. After a control period of five days during which the dosage of neostigmine was constant, mestinon was substituted. The improvement was dramatic. Both patients were able to sleep unmolested from 10 P.M. until 6 A.M., at which time their general muscle strength was slightly better than during the control period.

A survey of the results of this small clinical trial of mestinon in the treatment of myasthenia gravis suggests the following:

(1) 60 mg. of mestinon produces slightly greater improvement of muscle strength than 15 mg. of neostigmine.

(2) The onset of action of mestinon is slower than that of neostigmine. This may be partly accounted for by the delayed absorption caused by the sugar coating on these new tablets, which has since been discontinued.

(3) The effect of one tablet of mestinon lasts about half as long again as that of neostigmine. This was supported by a similar finding with intravenous injection.

(4) The incidence of abdominal colic is less with mestinon.

All these findings indicate only a minor improvement on a drug which, for the last twenty years, has played a revolutionary part in the treatment of myasthenia. The greatest usefulness of mestinon would appear to lie in the increased duration of action, which is particularly beneficial in the severely ill patient. It might also offer a satisfactory alternative treatment to neostigmine, especially if the latter produces troublesome side-effects.

Our thanks are due to Roche Products Ltd. for supplies of Mestinon.

St. Thomas's Hospital
London S.E.1

H. C. CHURCHILL DAVIDSON

Royal Free Hospital
London, W.C.1

A. T. RICHARDSON

TREATMENT OF ACTINOMYCOSIS WITH HYDROXYSTILBAMIDINE

SIR,—The report by Dr. Wolff and his colleagues (May 14) on the successful use of hydroxystilbamidine in severe infections due to *Candida albicans* prompts me to record a case of actinomycosis in which the drug was successfully used.

A married woman, aged 40, consulted me in July, 1952, on account of pain in the left hypochondrium for which no immediate cause could be found, although in the past she had suffered from anæmia and dyspepsia, and also pyelitis due to *Escherichia coli* and associated with slight one-sided hydronephrosis.

About eight weeks after she was first seen a painful swelling developed over the left ribs which had the characteristics of a cold abscess and was suspected of being tuberculous. As the swelling did not resolve it was ultimately explored, a small amount of grumous material evacuated, and the wound closed without drainage; no tubercle bacilli or other microbes could be identified in the material removed. A low-grade fever persisted and she remained generally ill. A month after the operation the wound broke down and a small amount of purulent discharge appeared which on two occasions contained the characteristic golden yellow granules of actinomycosis. Through an unfortunate hitch these granules were not cultured, but the true nature of her long illness was now obvious.

During the latter part of 1952 she was still very ill with general malaise, fever, cough, and foul sputum, with occasional hæmoptysis. X-ray examination of her chest showed some mottling of the left base with collapse, and the appearances suggested actinomycosis. She also had an indurated mass on the right side of the pelvis and a similar one in the left hypochondrium.

Once the correct diagnosis was made she was treated continuously for ten months with massive doses of penicillin and iodides, without appreciable effect. Towards the end of 1953, over a year after she was first seen, her general condition was so grave that it was considered by all concerned that no further treatment was practicable.

Because of the known in vitro action of hydroxystilbamidine on this type of organism it was decided to try the drug, so in December, 1953, she received ten daily injections of 225 mg. each intravenously dissolved in 10 ml. of distilled water, and later after a pause of three weeks in January, 1954, she had a similar course which was equally well tolerated. After this treatment began her temperature fell and her condition improved steadily until the end of the second course, by which time it was apparent that her main infection had been mastered. Unfortunately in February, 1954, a small abscess suddenly developed over the right ilium, which pointed and was opened; only *Staphylococcus aureus* was identified from the pus, and after a course of aureomycin her temperature fell and the local condition cleared up.

Following the new treatment the general improvement in her condition was astonishing and now, a year later, she has put on 3 stone in weight and can do a full day's work. No physical signs remain.

The history of this patient emphasises once again how the pleomorphic lesions of actinomycosis make precise diagnosis in its early stages so difficult; it may not be until there is a dramatic event, such as the production of the characteristic pus from a surface lesion, that the diagnosis is confirmed, however much it may have been suspected.

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[1] See *Lancet*, 1954, ii, 800.

Some cases show a partial response to iodides and penicillin in their early stages, but abdominal infections generally relapse, unlike infections around the jaw In 1939 I treated with iodides a case in which the cervical lymph-glands on one side were chiefly involved, the patient is still alive and free from symptoms In the patient I have now described, modern conventional treatment had little or no effect on the course of the disease, so it is all the more striking how two fairly short courses of hydroxystilbamidine brought the whole disease to a standstill except for the final incident of the superficial staphylococcal abscess, not an unusual event in chronic granulomatous conditions

The original source of the infection in this case may have been a young cat with discharging sinuses round the lower jaw which refused to heal The animal was destroyed without an exact diagnosis being made

Coltishall, Norfolk **BASIL J HANCOCK**

TREATMENT OF CHRONIC AMŒBIC DYSENTERY

SIR,—Although Dr Andrade (March 26) feels it is a misapprehension, destruction of cysts is an important aim in the treatment of amœbic dysentery especially if the disease is to be eradicated

It is common experience that treatment aimed at destruction of amœbæ or the cysts singly does not eradicate amœbic dysentery in all cases, but combined treatment more often does so Relapses with an amœbicidal drug like emetine are all too common, and carbarzone by itself will not satisfactorily cure amœbic dysentery It appears that unless both cysts and amœbæ are destroyed some of the cysts may develop into amœbæ before they are excreted and thus restart the infection This could be avoided by prolonging the course of the amœbicidal drug indefinitely, but in practice this is not possible because either the drug is too toxic or the amœbæ become too resistant to it Hence the necessity for combined treatment

It is hardly accurate to call the cysts harmless Their harmlessness either to the host or, through contamination, to the contacts cannot be guaranteed

Lucknow **INDER SINGH**

NON-PROGRESSIVE BREAST CANCERS

SIR,—I beg leave to make a correction of a point in my letter of May 14 My colleagues have shown me that, in attempting to adjust for the contribution which non-progressive lesions in stage 1 make to the five year survival-rates of various series (in the third paragraph of my letter), I made a fundamental error That error accounts for what appeared to be the close approximation of the net five year survival rates to what might be found in untreated lethal breast cancers I must, therefore, withdraw unconditionally that part of my letter dealing with that fallacious adjustment I think, however, that the other evidence, in itself, is sufficient to establish the non progressive character of the majority of stage-1 cancers

It is opportune now to quote the recent summary statement, among others, of Dr George Crile, jun, of the Cleveland Clinic Foundation "All evidence points to biologic predetermination and resistance of the host as the most important factors in the survival of patients with cancer of the breast [1]" And, in commenting on Crile's criticism of some radical surgery, Dr Morris Fishbein says [1] "This view is based on honest recognition of our lack of knowledge or of certainty in distinguishing inoperable cancers from those that are operable"

Department of Epidemiology and
Biometrics School of Hygiene
University of Toronto

N E McKINNON

Postgrad med J 1955 17, 280, 338

HEREDITY AND RHEUMATIC FEVER

SIR,—I should like to comment on one or two points in your annotation of March 5

You say that the children in our study [1] came from families of satisfactory economic status, and were in consequence not universally exposed to hæmolytic streptococcal infection But in fact they attended public schools and were not segregated, and Epstein [2] found that the incidence of respiratory infections was the same in the susceptible as in the non susceptible families.

We have not noted a decline in rheumatic fever among our patients A comparative analysis of the recurrence-rates during the past ten years has not revealed any significant difference from that observed in the previous ten years In addition, comparison of the incidence of severity, and of the duration of active carditis, during the years 1930–55, revealed a remarkable constancy

Diagnostic criteria undoubtedly vary from place to place However, the limited value of the postero-anterior radiographic view is now widely recognised, and the additional information afforded by examination in the oblique position should make comparisons more legitimate

We certainly expect some additional cases in the years to come, but since the size of our families will also probably increase, the predictions are unlikely to be altered significantly This was found to be true in the follow-up of our first series of families [3]

The New York Hospital,
New York, 21

MAY G WILSON.

PROFESSIONAL SECRECY

SIR,—My attention has been drawn to a communication [4] from the Ministry of Health, dated May 10, 1955, addressed to regional hospital boards and hospital management committees concerning carnal knowledge of mental defectives This memorandum describes the new procedure to be adopted when a certified mental defective is found to be pregnant, or there is reason to think that sexual intercourse has taken place

A previous memorandum on this subject advised that a report should be submitted to the Board of Control, but that the local police should not be informed The new memorandum repeats the advice of reporting the facts to the Board of Control but reverses the advice on communication with the police It states that "the Ministry is of opinion that it is desirable that in future such cases should be reported to the Police not necessarily with a view to prosecution but to enable the Police in consultation with the Medical Superintendent to decide what is the best course to take in all the circumstances" It concludes that medical superintendents should send reports to the local chief constable even where the offence has been committed in another police area

The current policy of the British Medical Association concerning professional secrecy is expressed in the following terms

> "It is a practitioner's obligation to observe strictly the rule of professional secrecy by refraining from disclosing voluntarily without the consent of the patient (save with statutory sanction) to any third party information which he has learnt in his professional relationship with the patient"

Unfortunately the advice now tendered by the Ministry of Health has apparently been prepared and issued without any prior consultation with the British Medical Association or any of the defence bodies who are materially interested in this matter for the protection of their members Furthermore reasons have not been advanced to justify the change of advice and the abroga-

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1 Wilson, M G, Schweitzer, M. *Circulation*, 1954 10, 699
2 Epstein N *Amer J Dis Child* 1954 87, 600
3 Wilson, M. G, Schweitzer, M. D, Lubschey, R *J Ped*
1943 22, 468, 581
4 H.M (55)46

ion of the rule of professional secrecy in the case of mental defectives.

There may well be occasions when it would be fitting and proper for the police to intervene by the institution of legal proceedings against a suspected offender and there may also be sound reasons in law for issuing the advice described above. I feel, however, that before a change of this order is sponsored by official Governmental departments relating to an important ethical tenet the least that the Association could expect would be a communication from the parties who propose an alteration setting out their reasons and any legal sanction that might be invoked for their support. I hope that opportunity will be afforded in the near future for representatives of the Association and of the Ministry to meet to discuss the situation created by the issue of the memorandum.

The Medical Defence Union,
London, W.C.1

ROBERT FORBES
Secretary

ESTIMATION OF BLOOD-LOSS

SIR,—Your editorial of May 14 on the difficulty of estimating accurately the amount of blood lost at operation or as a result of trauma was excellent—until its close. Having rightly stressed that blood loss is usually underestimated, you continue: "... there is still insufficient evidence to justify the very large transfusions of blood recommended by Prentice et al. Early surgical treatment should be combined with rapid transfusion of enough blood to maintain the blood-pressure within normal limits." But one of the reasons that Prentice et al. gave these very large quantities of blood was to do this very thing. And surely the fallacy of relying only on the blood-pressure as a measure of circulatory normality is the reason why blood loss is so frequently underestimated. This recurrent canard is continually being shot down, and some of the best shots are included in the references to your editorial. These references point out that a loss of blood volume of up to 2 litres can be associated with a normal blood pressure. They point out that such patients are liable to develop alarming and sometimes lethal falls of blood pressure under anæsthesia, and there is also evidence that they are liable to develop acute anuria.

The temperature and colour of the nose and extremities and the size of the subcutaneous veins are far better clinical indications of the normality of blood flow than is the blood pressure. Prentice and his colleagues were aware of these facts, which is another reason why they gave such large quantities of blood. Finally, the group which they transfused included many suffering from multiple gunshot wounds which continued to bleed until and during operation. It is unfair to criticise the quantity of blood (10–20 litres) found necessary in these cases, by contrasting them with the amounts found to be adequate for civilian casualties with closed injuries or a single open lesion.

St Thomas's Hospital
Medical School,
London, S.E.1

H. E. DE WARDENER.

CORPORAL PUNISHMENT IN SCHOOL

SIR,—Dr Jackson's letter of May 14 sponsors a point of view that has been carried to absurd and dangerous extremes in the United States. Without commenting upon his *gestalt* theories I feel compelled to warn British readers that the "permissive" attitude can lead to serious lowering of intellectual and moral standards in schools.

A Californian teacher has recently been discharged not for using corporal punishment, but for teaching reading by "traditional" instead of "progressive" method. He testified that fourth grade children do not know the alphabet, and that when he attempted to teach the multiplication tables by drills he was rebuked by a superior. The teacher was not allowed to discipline a boy who called him obscene names for three months. Another teacher was not allowed to punish a child who attacked her and broke her nose. The "progressive" school authorities would not listen when these and other teachers sought disciplinary measures.

Dr Jackson's *gestalt* theories lead him to believe that punishment will render children susceptible to illness. Years of experience with "progressive education" convince me that lack of intellectual and moral discipline can be a serious danger to children, to the community, and, ultimately, to the survival of all civilised values.

Edinburgh.

RONALD W. ANGEL.

ADENOSINE TRIPHOSPHATE IN PAROXYSMAL TACHYCARDIA

SIR,—In 1929 Drury and Szent-Györgyi[1] pointed out that adenosine triphosphate (A.T.P.), adenosine monophosphate (A.M.P.), and adenosine dilated the coronary arteries and slowed atrioventricular conduction. The work of Green,[2] Bielschowsky et al.,[3] and others made it clear that these substances act by inducing a "shock" comparable to that produced under certain conditions by histamine, adrenaline, or insulin. Moreover, it was found that the adenyl root is responsible for the vasodepressor effect, while the pyrophosphate is the shock-inducing factor in A.T.P.; also that magnesium phosphate is the most active shock-inducing member of this group of substances.

Accordingly I have tried, over the past ten years, to bring about the cessation of paroxysmal tachycardia by producing a mitigated shock with intravenous adenosine triphosphate. 18–20 seconds after an intravenous injection (given as rapidly as possible) of 2 ml. (20 mg.) of A.T.P. complete asystole lasting 2–4 seconds usually ensues. This asystole is sometimes interrupted by ventricular extrasystoles originating from various foci or by isolated auricular contractions. In these circumstances the patient is asked to swallow once or twice, and subsequently he reports with relief that his galloping heart action has slowed down. The electrocardiogram (E.C.G.) shows a nodal impulse formation for 3–4 complexes or, after a few atypical auricular ventricular complexes, transitional auricle activity without ventricular stoppage. Subsequently regular sinus rhythm is established, differing from normal rhythm only in that the conduction time from auricle to ventricle is longer; but after 3–4 complexes this too returns to normal.

Judging from the E.C.G. changes during the injection there seems no doubt that the A.T.P. substances arrest the heart action and temporarily cause complete asystole. While the impulse formation is slowly recovering they inhibit impulse conduction and so prevent recurrence of the paroxysmal tachycardia.

The effective dose is 20 mg. (2 ml.), provided that the vein is sufficiently wide to allow rapid injection. If the veins are thin and weak walled, I administer 30 mg. at the outset. In no case have I observed any toxic side-effects. Since the effect is due to the high blood level, intramuscular injection is unsuitable.

In 1947 I reported 90 onsets successfully treated in this way,[4] and in 1949 an additional 118 onsets.[5] Komor and Garai[6] last year reported success in 250 episodes among 50 patients.

The response of supraventricular paroxysmal tachycardia to adenosine triphosphate is so striking that it may be taken as one of the chief criteria in the diagnosis of the condition.

Postgraduate Institute of Medicine,
Budapest, Hungary.

FRIGYES SOMLÓ.

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1. Drury, A. N., Szent-Györgyi, A. *J. Physiol.* 1929, 68, 213.
2. Green, H. N. *Brit. med. Bull.* 1945, 3, 10.
3. Bielschowsky, M., Green, H. N., Stoner, H. B. *J. Physiol.* 1946, 104, 239.
4. Somló, F. *Orv. Lapja*, 1947, 3, 1431.
5. Somló, F. *Fővál. Ter. Kórház Évkönyv*, 1949.
6. Komor, K., Garai, Y. *Orv. Hetil.* 1954.

FEAR OF CANCER

SIR,—I read with interest Mr Donaldson's article in your issue of May 7, and I should like to mention two aspects of the fear of cancer which add, I believe, in many instances not inconsiderably to the mental suffering of patients and to the distress of those around them These apprehensions are that cancer is contagious and, again, that it forbodes malignancy in the offspring

In the case of a man who was under my care some years ago the differential diagnosis between bronchial carcinoma and lung abscess could not be settled The patient's wife asked whether it was necessary for her to take precautions in case the illness proved to be cancer I told her that cancer was not contagious, but she was unconvinced When the patient died his wife was the first to speak about a postmortem examination, and on hearing that an abscess had been found in the lung, but no cancer, her face lit up with relief and she exclaimed "Thank God for that"

I am inclined to think the belief that cancer is infectious is a widespread and deeply rooted one It may be thought of as a modern version of man's primitive response to dangerous illness against which he used to protect himself by the system of taboo Since this system has no currency in advanced society, *tendencies* of avoidance entering into the attitudes towards the sufferer are bound to impart a sense of guilt which cannot but render the relation to him a conflicting one For his part, the sufferer who, of course, shares in the notions of the undeclared taboo senses his position as that of a fear-arousing outcast Here Mr Donaldson's personal experiences provide a telling illustration of how, in keeping with the rules of taboo, even the mention or alone the thought of cancer come under the restrictions of the ban

The notion of cancer heredity, looked at as an irrational belief, may be only an extension of the idea of its infectiousness

West Park Hospital,
Epsom Surrey

JOSEPH ZELMANOWITS

MEDICAL TELEVISION PROGRAMMES

SIR,—We are sorry that Mr Welsh (May 14) was revolted by the television programme of May 2 on *Mind and Body* Human physiological demonstrations can only be made on living subjects In this programme all three subjects were professional associates of the doctors taking part We fail to see how the first two simple demonstrations of physiological response to stress could appear revolting The cigarette "burn" was used to demonstrate that the physiological response to a threat can be greater than the stimulus itself The "burn" was not only suggested as a suitable stimulus by the subject (himself a doctor) but was accepted by him quite willingly on a number of occasions during rehearsals Of course the only contact made was a light touch, producing no more than erythema

Some people have reported to us that they themselves experienced a feeling of mounting tension whilst observing the threat, and it is clear that it was this communicated anxiety that they found disturbing We have yet to meet anyone to whom it had even occurred that "sadism" was a motive in presentation, and perhaps if he had not switched off at a crucial moment Mr Welsh would not have retained a distorted impression

To judge by correspondence received by the B B C, there has been no general adverse public reaction Indeed, two general practitioners have reported to us that, since viewing the programme, patients of theirs have been able to accept the emotional basis of some of their somatic symptoms and have requested psychological help

The educational value of television programmes on appropriate medical subjects has recently been referred to in your columns,[1] and we hope that the B B C will continue to present interesting and useful medical programmes The technique is still developing and we feel that much remains to be learnt about the proper balance between demonstration and explanation necessary to avoid misinterpretation

In order that, as broadcasters, we may continue to maintain our anonymity we sign ourselves,

Dr A, Dr B, and Dr C

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1 *Lancet* 1954, ii, 279

TOXIC EFFECTS OF RESERPINE

SIR,—We read with interest the letter from Dr Stead and Dr Wing in your issue of April 16 on the toxic effects of reserpine They describe two cases of parkinsonism developing during treatment with large doses, but they suggest that toxic effects are slight with small doses

In our experience of mentally ill patients treated on dosage of 0 5–2 mg daily, side effects may be troublesome The degree of disturbance varies widely but is generally greater in the neurotic than in the psychotic Drowsiness, loss of energy, nasal stuffiness, and tremor are commonest, and are most marked at the end of the first and during the second weeks of treatment Aches in the limbs occur infrequently Unless warned of these effects, many outpatients may stop the drug before there is any chance of benefit Wilkins[1] has reported the development of agitated depression in cases of hypertension treated with reserpine

Frequently the side effects may so add to the burden of the patient with endogenous depression, that admission to hospital may be necessary We feel that in these cases the drug is contra-indicated We have noted the development of parkinsonism in some cases treated with oral dosage of 4–8 mg daily for one to three months Facial immobility and restlessness are common on this dosage Elderly patients may easily become tremulous and unsteady with consequent danger of fractures Frequency of micturition is fairly common and nocturnal incontinence of urine has been noted in some cases Increase in dreams pleasant or unpleasant sometimes occurs Kline has reported that 2% of patients treated with reserpine have epileptic convulsions for the first time, but we have not observed this in any case

Our experience with parenteral reserpine has been mostly in a series of 25 inpatients who were given 10 mg intramuscularly and 3 mg orally daily for three to seven weeks. Drowsiness, loss of energy, nasal stuffiness and restlessness occur in every patient to some degree Drowsiness may be so bad that most of the day is spent in bed. Nasal congestion may be complicated by nose bleeds or much less commonly by necrosis of nasal mucosa or sinusitis or headaches possibly due to vacuum changes in the sinuses Breathlessness and a sensation of smothering may occur Restlessness may reach a degree in which rest is unattainable without heavy sedation and may bring about impulsive behaviour Impaired mobility of facial expression and increased salivation are common Parkinsonism to the degree described by Wing and Stead has been noted in 5 of the series

Kline[2] does not consider this a contra indication to continued treatment and in this we concur Reduction of the intramuscular dosage to 5 mg daily usually provides relief when the patient is unable to get about freely or to feed himself Sometimes the patients complain of pain in the back of the neck or in the lumbar region, or of aches in the limbs Appetite is usually increased, but where side effects are marked may be greatly reduced We have noted also in individual cases postural hypotension and unexplained œdema of the feet and ankles Delay in initiating micturition and impairment of accommodation may occur to a minor degree The 10 mg injection is 4 ml in volume and is frequently painful

It is evident that parenteral reserpine therapy in this dosage can be a very unpleasant treatment We hope that modifications in the régime will make it less [illegible] Patients require frequent encouragement and explanation Adjustment of dosage is fairly often necessary

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1 Wilkins, R. W *Ann N Y Acad Sci* 1954, 59, 36
2 Kline N S Address to American Psychiatric Association, Berkeley, California, Dec. 30, 1954

We have found barbiturates best in the control of restlessness, an 'Antistin Privine' nebuliser for nasal congestion and a belladonna mixture for excessive salivation. Despite these disadvantages our results have been such as to encourage us to continue trial of the drug.

We are indebted to Ciba Laboratories Ltd. for supplies of reserpine in the form of 'Serpasil' and for supplies of 'Antistin Privine.'

J N P MOORE
E A MARTIN

St. Patrick's Hospital, Dublin.

CORTISONE, CORTICOTROPHIN, AND INFECTION

SIR,—The most enlightening paper by Dr Shaper and Dr Dyson (April 30) prompts me to draw attention to the relationship of an allied drug (hydrocortisone) to infection. In view of the increasing popularity of the use of hydrocortisone in local treatment of joint and soft tissue lesions it may be timely to report a case of suppurative arthritis after an intra-articular hydrocortisone injection.

A woman of 75 was admitted to hospital with an infective arthritis of her knee. She gave a six weeks' history of general malaise followed by pain and swelling of her right knee. Two weeks before admission she attended the outpatient department of another hospital where physiotherapy was ordered and hydrocortisone was injected into the knee-joint. Following this her condition deteriorated.

On admission she had a mild pyrexia and a moderate effusion in the knee joint with restricted movements. Thick pus was obtained on aspiration of the joint, which had to be incised. The culture yielded a profuse growth of penicillin-sensitive pneumococci. The infection subsided completely with local and systemic penicillin.

There are three possible causes of the joint infection:

(1) She had a pneumococcal lung infection with secondary pneumococcal arthritis, the hydrocortisone causing the latter to flare up.

(2) The knee condition was an exacerbation of an osteo-arthritis and the pneumococci were introduced during the hydrocortisone injection (unlikely).

(3) She had a non-specific "toxic" synovitis following pneumonia. The trauma of the injection and the hydrocortisone in the joint caused a *locus minoris resistentiae* and the deposition of pneumococci in the joint.

The first is the most likely explanation, but if the last be true intra-articular hydrocortisone should be contra-indicated not only in an infective joint lesion but also in the presence of an infective focus elsewhere.

Clatterbridge Hospital,
Bebington, Cheshire

E H STRACH.

STAPHYLOCOCCAL INFECTION IN THE NEWBORN

SIR,—I have followed the recent correspondence with interest and I note that Dr Forfar and his colleagues (May 21) have now referred to what are probably the most important aspects—namely, the unsuspected pathogenicity and the prevention of staphylococcal infections in the newborn. That certain staphylococci can be dangerous was realised last century when Ogston, the illustrious discoverer of the organism, suffered from a lung abscess which yielded a pure culture of staphylococci. His remark that he had hitherto regarded the staphylococcus as a "friendly little chap" is still echoed today. The unfriendly strains can now be differentiated with reasonable accuracy by phage-typing, but it must be confessed that facilities for typing are not readily available to everyone investigating staphylococcal outbreaks. This is particularly unfortunate since it makes it impossible to confirm the route of infection.

Dr Forfar and his colleagues rightly suspect that the new arrival in the household may introduce a virulent (and resistant) organism acquired in the maternity hospital. Within twenty-four hours of its residence in the hospital nursery the infant acquires the flora and fauna of its fellows, and it is capable of infecting the mother's breast with any pathogenic staphylococci present in its nasopharynx. The evidence of this has been conclusively demonstrated by Colbeck[1] and confirmed by Isbister.[2] I am indebted to these investigators for their personal communications which solved the problem of why the incidence of mastitis was infinitely higher in mothers who had been confined in the Burgh maternity hospital than in those confined at home. It is probable that a household may become tolerant of its own domestic strain of the staphylococcus without developing any resistance to others.

That is why congregation in hospitals carries such risks and why the nursery—where such still exists—is the danger spot, nullifying as it must the most rigid precautions applied to the mother alone.

While I endorse the first part of Dr Forfar's remark that "prevention, not treatment, of neonatal staphylococcal infection must be the ultimate goal," but as yet that appears to be unattainable, I think that he might be disposed to amend the latter part after he has put into practice the principle of strict cubicle isolation of the mother *with* her infant.

Health and Welfare Department,
Kirkcaldy

J R W HAY

HASHIMOTO'S STRUMA LYMPHOMATOSA AND RIEDEL'S THYROIDITIS TREATED BY RADIUM

SIR,—I was interested to read that Dr Cooke and Dr Luxton (May 7) "have studied about 25 patients, in nearly two-thirds of whom the diagnosis has been confirmed by histological section," "that not infrequently the patient first visits her doctor for symptoms not quickly ascribed to thyroid disturbance, such as lassitude, muscle and joint pains, increasing weight, and changed facial appearance," and that "the efficacy of modern treatment by oral dried thyroid emphasises the need for the diagnosis of Hashimoto's disease to be considered more readily." I was particularly interested in their remark that "one of our patients, observed for seven years, now has a liver which is greatly enlarged."

In a paper[3] in 1938 by J Mill Renton and A A Charteris I contributed to a report on 5 cases which had been treated successfully with radium (1800r–4000r) and remained well, to the time of reporting, for from two to five years. Of these 5 cases 3 were diagnosed on histological evidence and 2 on clinical and therapeutic grounds, the response to radium being so astonishingly rapid, without local or general reaction, and quite unlike that given by any other condition.

Our definition of Riedel's thyroiditis included "struma lymphomatosa" and "lymphadenoid goitre," and our cases 1 and 4 were of this state confirmed histologically. They were middle-aged women who complained of discomfort and swelling in the neck with dysphonia and dysphagia; tissue was removed from the isthmus of the gland. Following a mistaken histological diagnosis of malignancy in case 1 a radium collar was applied (2500r) and within ten days the patient was symptom-free and within thirteen days the thyroid swelling had gone. On account of such favourable and ready response 3 other cases were treated with radium; in 2 a biopsy specimen was taken, but in 1 treatment was begun after a clinical diagnosis of Riedel's thyroiditis had been made, and a like response to radium was considered *diagnostic*.

The 5th case was culled from the records, having been diagnosed clinically as thyroid carcinoma and given a palliative dose of radium estimated to be 1800r. She showed great improvement of voice, and the neck swelling subsided at the end of a week. As she was alive and well almost five years later, when we reviewed the hospital records prior to publication, she was considered to have suffered from Riedel's thyroiditis.

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1. Colbeck, J. C. *Canad med Ass J* 1949, 61, 557
2. Isbister, C. *Med J Aust* 1954, ii, 801
3. *Brit J Surg* 1938, 26, 31

These patients all remained well for many years and none showed any signs of thyroid deficiency We considered that the radiation destroyed the lymphocytes and germ centres that form in the thyroid gland and infiltrate the overlying muscles, and that the thyroid tissue, having been overrun by these cells and become atrophic, had regenerated satisfactorily, from the absence of later pressure effects we concluded that fibrosis had not occurred

The late results of the cases have been given me by Dr Charteris, of the Western Infirmary, Glasgow, from his follow up notes, and the short series in brief is

Age	*Variety*	*Treated*	*Result*
39	Hashimoto	1933	Well for at least 18 yr
50	Riedel	1934	Well for 19 yr
49	Riedel (clinical diagnosis)	1935	Well for 15 yr
43	Hashimoto	1937	Well for 18 yr
72	Thyroid carcinoma (clinical diagnoses)	1933	Well for 20 yr (Died at 92 of senile vascular disease)

Although we were unable to contribute to an understanding of the ætiology of the condition, we reported a simple and harmless diagnostic test which is also an effective therapeutic measure

North Middlesex Hospital,
London, N 18 J F HEGGIE

HYDROCORTISONE OINTMENT

SIR,—I was most impressed by the account in your issue of May 21 by Dr Brian Russell and his co-workers of their valuation of hydrocortisone ointment in the treatment of various pruritic dermatoses. Dr Russell and his team are to be congratulated on their scientific method of approaching the problem, and for the clarity of their results, which showed in which conditions the use of hydrocortisone ointment is indicated

It is interesting to note that these appear to be mainly those classified in Sneddon's[1] group 2—"dermatoses with a large psychogenic factor"—and, as I have written elsewhere,[2] it is of the utmost importance that any underlying emotional (or psychogenic) factors be carefully sought out and discussed with the patient, in addition to local or symptomatic treatment

This does not detract from the usefulness of hydrocortisone ointment, however, and I hope that it will very soon be available for those patients remaining under the care of their general practitioners as well as for those who are referred to hospital outpatient departments

London N W 3 PHILIP HOPKINS

THE CARAVAN SITE

SIR,—May I comment briefly upon one of the points discussed in your article of April 30 (p 924)?

You refer to control of caravan sites, and state that "it is better that the site owner should run his own business in an orderly and efficient way than to make bad laws to suit hard cases" I accept this platitude, but why should new laws be "bad laws"? What happens when the site owner fails to run his business in an orderly and efficient way? The health of the community is at stake Why should owners of badly managed, unhygienic sites be unchecked? Should we wait until news of a dysentery-typhoid outbreak strikes the headlines and then, deploring this unfortunate occurrence, assure the public that every possible effort is being made to limit the spread of infection? Surely, if caravan sites can be made into healthy and attractive holiday centres, which I believe practicable, slum conditions should no longer be tolerated Taking into consideration the present high rate of caravan production, I believe the negative policy of *laissez-faire* is likely to lead to the situation getting completely out of hand

Good sites should be encouraged by every possible means They are entitled to get a reasonable financial return for their outlay and expenditure in building up and maintaining high standards and should not necessarily have their activities curtailed in the winter months. The neglected sites, if they fail to raise their standards should be subjected to slum clearance

For the reasons detailed in my article[1] I consider that amendment of the Public Health Act, 1936, is essential

Newcastle upon Tyne WILLIAM HUNTER

A VISIT TO KOLTUSHI

SIR —I should like to reassure Dr Mungo Douglas (May 21) that I do not wish to dispute the discovery to which he alludes, although I must confess I was unable to grasp its meaning Since it prevents disturbances of gastric function, bronchospasm, and schizophrenia, one awaits confirmation with interest However, the purpose of my letter was to object to vague disparaging remarks about the work of Pavlov which, in my opinion, holds promise of clinical application in such diverse fields of medicine as indicated by the three disturbances mentioned at random If Pavlov was unaware of the work of Mr Alexander it may be regrettable, but it does not invalidate Pavlov's theories or, still less, his experimental findings However notable the claimed discovery may prove to be, it does not excuse the use of disparaging remarks about the work of others unless such remarks can be substantiated by demonstration of specific errors of scientific fact

Sheffield C H FOGGITT

CLINICAL STAGING OF CARCINOMA OF THE BREAST

SIR,—I would be grateful if you would allow me to comment upon the response to my letter in your issue of March 26 and in the *British Medical Journal* of the same week A copy of the letter and a covering note were sent to a surgeon and a radiotherapist at each of the teaching hospitals in Great Britain and to a number of interested clinicians In all, 65 people were written to and I asked not only for their personal views but suggested that they might feel inclined to bring the matter forward for discussion at their hospital medical committees 43 replied, with varying degrees of enthusiasm, that they favoured the plan to establish an international staging and wished me luck, though several said it would be an uphill struggle 2 said it was hopeless trying and 1 said the attempt should not be made at all The opinions most frequently expressed were that the British Empire Cancer Campaign, the Royal College of Surgeons, and the Faculty of Radiologists were the most appropriate bodies to deal with the matter Mr Blaikley (April 16) has informed your readers (and this has also been pointed out to me by individual correspondents as well as by the reports from medical committees which are beginning to reach me) that a committee of the General Register Office under the chairmanship of Dr A H T Robb-Smith is considering this subject at the moment

It seems, therefore, that the problem is actively exercising learned opinion and it is certainly not the wish of my colleagues at the Royal Marsden Hospital, on whose behalf I first wrote, to complicate the issue further at present

I think it is generally agreed that any staging must be clinical although, as Dr Bloom and Dr Richardson point out,[2] a pathological staging of the regional lymph nodes is much more accurate But it is a fact that this information is not available in a high proportion of the cases, and their graph indicates that within each clinical stage what one loses in pathological grade 3 cases one gains in grade 1 cases My personal view is that staging should only be clinical but that in the presentation of results the histology should also be considered when this is known Dr Robert Morrison s staging[3] employing as it does eleven groups, looks complex but is in fact an application of the TNM system which will undoubtedly form the basis of any international staging not only for cancer of the breast but for other sites as well I feel confident myself that an acceptable staging will emerge in the not too distant future

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[1] Sneddon, I B *Brit med J* 1949, i 472

[2] Hopkins, P *In* Modern Trends in Psychosomatic Medicine Edited by D O'Neill London, 1955

[1] *Med Offr*, 1955, 93 179

[2] *Brit med J* May 21, 1955, p 1276

London W 1 MICHAEL HARMER

REACTION TO VITAMIN B_{12}

SIR —I read with interest the account by Dr Gillhespy of a patient in whom an injection of vitamin B_{12} produced an anaphylactoid reaction with urticaria of the skin

In 1952 I reported[4] that whereas side-effects occasionally occurred following the administration of certain preparations of vitamin B_{12} derived from cultures of *Streptomyces griseus* there were no adverse reactions to a preparation of vitamin B_{12} derived from liver

It would be of interest to know the nature of the vitamin B_{12} preparation which produced the sensitivity reaction in Dr Gillhespy s patient

Cowley Road Hospital
Oxford. P D BEDFORD

INFORMATION FROM HOSPITAL

SIR,—Working in the vicinity of several of the teaching hospitals I am impressed by the frequent complaints from relatives of inpatients and from outpatients themselves that they find it almost impossible to obtain adequate information from the hospital about their progress and about the proposed investigations and treatment Whilst I always find house officers extremely cooperative when asked for information over the telephone this is a time-consuming business both for them and for me

Would it be worth appointing a general practitioner to each large hospital whose sole and very much full time function would be to act as a medical liaison and information officer and who would always be available to those patients, relatives and general practitioners in the district needing immediate clinical details rather than the usual nurse s bulletin ?

London S W 7 BENJAMIN LEE.

DRUGS IN THE TREATMENT OF DEPRESSION

SIR —Your annotation of May 21 does not mention opium I think this is still a valuable drug in the treatment of minor depressive syndromes many of them with anxiety, which are so commonly seen in psychiatric outpatient practice It may be dispensed in the form of a mixture containing 10 minims of tincture of opium (B P) to the half ounce of chloroform water (its constipating effect being offset by the addition of a few minims of liquid extract of cascara) taken thrice daily Its soothing effect is as great as that of the barbiturates though not produced so rapidly

I have been prescribing a mixture of this kind for many years. I have never seen a patient become addicted to it (it is extremely unpleasant to take) and only once to my knowledge has a patient attempted to use it for ostensible suicidal purposes. He swallowed an estimated quantity of six ounces of the mixture slept for about fourteen hours, and woke up feeling better than he had done for months.

Considering too the ease with which patients may hoard barbiturate tablets or capsules and the frequency with which they are used in suicidal attempts, I think there is still much to be said for the old fashioned opium mixture Dispensed in the strength I have mentioned the mixture is not subject to the Dangerous Drugs Regulations It can be used safely for many weeks at a time and it goes well with the amphetamine group of drugs I have generally found that it is only when insomnia is severe that it is necessary to add a nocturnal barbiturate to this régime

Warneford Hospital
Oxford IAN SKOTTOWE

REGISTRARS AND REGISTRARS

SIR —If for some my letter of April 23 expressed malevolence I can only retort as did the mediocre marksman at the firing point Well Sarge it left here alright !" A Letter to the Editor may appear in various styles and if a correspondent thinks it more effective to make his point with very obvious exaggeration and a bit of fun poking surely it is in accordance with accepted practice—particularly if the subject is a political one

May I take the opportunity of repeating the previous theme that registrars at the periphery—registrars (P) if you like—deserve far more encouragement

REGISTRAR (W PLUS)

METCHNIKOFF, LISTER, AND EHRLICH

Dr Leonard Crome honorary secretary of the medic committee of the Society for Cultural Relations with th U S S R (14, K[illegible]on Square London W 8) writes

A requ[illegible]come to the Society from the Metchnikoff Museum in [illegible] U.S.S.R for information concerning the whereabouts of letters from Metchnikoff to Lord Lister and Paul Ehrlich We should be most grateful if any of yo readers could help us to trace these letters.

Medicine and the Law

Damages for Rheumatoid Arthritis

A Scottish school teacher has been awarded £20 damages against her employers the Glasgow Corporati for rheumatoid arthritis contracted through working unhealthy conditions[1]

The plaintiff a woman aged 28 averred that as a result s had become unfit for her professional duties and claim £10 000 damages. She said that the classroom in which s taught was badly ventilated and inadequately heated T corporation maintained that the room was not in an unhealt or dangerous condition and called medical evidence to t effect that conditions of damp and cold had no relevance considering the cause or aggravation of rheumatoid arthrit

The judge in summing up told the jury that there we three questions which they must decide The first w whether they held it proved on the evidence that the plaintiff teaching place was cold damp and ill ventilated throughou the whole period of two and a half years that she was ther If they were not satisfied that the room was unduly cold damp during that period then they must find for t defendants. If they were satisfied that the room was undu cold and damp then they must consider whether th conditions caused or aggravated the rheumatoid arthri from which the plaintiff suffered. The third question w whether the development of rheumatoid arthritis in t plaintiff was something that the defendants should ha anticipated from the exposure of the plaintiff to the conditio in the room. The law required that the plaintiff must pro that the defendants as ordinary reasonable people ought have anticipated and foreseen that if she was exposed to w and cold conditions rheumatoid arthritis was likely to caused or aggravated

The jury by a majority of seven to five found for t plaintiff on these three points and assessed the damages £*000

It is not yet known whether the corporation intend appeal This case is clearly of unusual interest

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[3] *Ibid* May 1955 p 1152

[4] Bedford P D *Ibid* 1952 i 690

[1] *Scotsman* May 19 1955

Obituary

DONALD YOUNG SOLANDT

M A, M D Toronto, Ph D Lond, D P H, F R.S (C)

Dr Solandt, professor and head of the department of physiological hygiene and professor of physiology in the University of Toronto, died on March 30 at the age of 48

He was born in Ottawa, Ontario, the son of the late Donald McKillop Solandt, D D He entered the University of Toronto in 1925, and after taking his M A in physiology he graduated in medicine in 1933 His keen interest in biophysical research led him to postgraduate work in the University of Pennsylvania and later in England, where he obtained a PH D degree from the University of London in 1936

On his return to the University of Toronto in 1936 he took up his duties as assistant professor of physiology, and in 1939 he was appointed associate professor and two years later to the chair of physiological hygiene He retained his appointment in physiology where he was in charge of the section of biophysics During the late war he served as surgeon commander in the medical esearch division of the Royal Canadian Navy, where he was responsible for many valuable researches on vision nd hearing and related biophysical subjects In recognition of this work, particularly on the protection of ight vision, the United States government awarded him he *Medal of Freedom* with bronze palm

Dr Solandt served on advisory committees of the épartment of National Health, the National Research ouncil of Car da, and the American Public Health ssociation e was a fellow of the Royal Society of anada and member of many scientific societies in anada, th nited States, and England He was an norary ow of the American Medical Association s boc *Highways to Health* appeared in 1933, and cor ted many papers on medical and biophysical ep scientific journals, including several to our n the early 'forties describing experimental f the anticoagulants

R N, who worked with Solandt in Toronto before e war, recalls him as "at first sight a rather shy rsonality, and quiet in speech and manner However, is reserve was superficial and anyone who worked with n soon found that underneath was a warm and veable character His leanings were essentially biolysical, though he was interested in the physiological pects of all branches of medicine, and was always lling to try out any experiment He did much of his rly work at University College Hospital and always d a soft spot for England and welcomed any opporunity to visit it again His integrity and keen sense of umour will be missed by his many friends"

C H B, to whom we are indebted for this memoir, lds "The breadth of Dr Solandt's interests was a urce of constant amazement to all who knew him is extensive knowledge of literature, music, natural ience, and photography made him an exceptionally imulating companion In his passing the university s lost a man whose professional services in science and education have been of the highest value"

Dr Solandt is survived by his widow, the former rbara Garrard of London, and three daughters

CORNELIUS ALBERT GRIFFITHS

F R.C S

THE death of Mr Cornelius Griffiths, on May 7, at the e of 90 ends the career of the oldest and one of the ost notable Welsh surgeons

He was born at Merthyr in 1865 and he studied at e medical schools of Bristol and St Bartholomew's ospital He qualified in 1880 and, after holding a use-appointment at Bristol General Hospital, he became edical tutor in the Bristol Medical School In 1893 he ok the F R C S, and the same year went to Swansea R M O at the General Hospital The following year mov o Cardiff and, in due course he was appointed of Cardiff Royal Infirmary

es "His work was of an outstanding forty years, scores of doctors were taught admired his technique. They also will remember his unfailing good manners under any circumstances, and his kindness to the students in private. In his earlier years at Cardiff he was constantly operating in all the coal areas round the city, and, as there were no motor-cars or ambulances, and only limited hospital facilities, he often operated in lonely farm houses by candle-light on the kitchen table In his retirement he found relaxation in his favourite Usk fishing, and for several years he sat on the magisterial bench. To everyone he was affectionately known as 'Corny,' and there are many who think of him not only as a great surgeon, but as the gentlest of men"

JAMES RANDAL HUTCHINSON

M D Manc, D P H

Dr Hutchinson, who retired in 1947 after nearly forty years as an epidemiologist at the Ministry of Health and the Local Government Board, died on May 6 at the age of 75

Hutchinson was a north-countryman, blunt and direct of speech After a brilliant career at Owens College, Manchester, he graduated M B with honours in 1902 Almost at once he decided to specialise in public health and in 1904 he took the D P H. Four years later he became senior assistant to Dr James Niven, medical officer of health for Manchester Under Niven he acquired great experience in the investigation of outbreaks of epidemic disease, especially those of enteric fever, and the administration of anti tuberculosis measures in which his chief was a pioneer

In 1910 Hutchinson became M O H for Wigan, but Sir Arthur Newsholme, medical officer of the Local Government Board, already had an eye on this reliable young investigator, and on his recommendation in 1911 Hutchinson was appointed a medical inspector of the board. Here he worked under the direction of Colonel R J Reece and quickly gained a reputation as an epidemiologist During the first world war his many investigations helped to safeguard the country from the dangers of epidemic outbreaks In 1919 he became a medical officer of the Ministry of Health working in the branch dealing with sanitary administration in relation to infectious disease, again with Reece as his chief and later with Macewen

In 1926 the Minister of Health, with the Medical Research Council, appointed a committee of experts to inquire into the preparation and standardisation of vaccine lymph, the methods of vaccination to be used, and the possibilities of removing any of the risks attendant on vaccination As secretary of the committee, Hutchinson was largely responsible for the two reports published in 1928 and 1930 which did much to allay public anxiety as to the risks of encephalitis after vaccination. Later Hutchinson became deputy senior medical officer of the branch concerned with tuberculosis and epidemic diseases and during the late war he served at headquarters as a specialist medical officer in epidemic diseases When he reached the retiring age he was re-employed as a temporary medical officer in the Ministry, where his experience and advice were of great value Before his final retirement, he contributed to the *Chief Medical Officer's Report for 1945* a valuable historical note on the prevention of smallpox in England and the foundation of the Government Lymph Establishment

A. S MacN writes "Hutchinson was of medium height, of fair colouring, clean-shaven, and somewhat reserved in manner, a worker of regular hours, methodical, reliable, and industrious He had his individual characteristics Towards the end of May each year he would discard his bowler hat, don an old-fashioned straw boater, and wear an alpaca jacket in the office We always said we could date the onset of summer by Hutchinson. He was a great believer in field epidemiology, and at first resented the more predominant part now played by bacteriologists in investigation of disease outbreaks. When convinced of their value, there was no more loyal worker and collaborator in the Emergency Public Health Laboratory Service. He carried the experience and thorough standards of the medical department of the Local Government Board into a more hurried and restless age He elucidated many problems in epidemiology and public-health administration and his work will not be forgotten"

Dr Hutchinson is survived by his widow

WILLIAM MORTON ROBSON

M D Lond., F R.C.P

Dr Robson consulting physician to Northampton General Hospital, died on May 10, at the age of 77, at his Northampton home.

He was born in co Durham and he studied medicine at Guy's Hospital qualifying in 1901 After holding residential appointments in London he went to St Andrew's Hospital Northampton, in 1903 as junior medical officer By 1905 he had taken the M D (with gold medal) and M.R C.P , and had been appointed to the honorary post of assistant physician in charge of the electrical department at the Northampton General Hospital.

Later he became radiologist to the hospital as well as physician It was largely thanks to him that an anonymous donor gave much of the present X ray department to the hospital "He was a first-rate clinician," R. O L. writes, "which helped him greatly in his radiological work, and for many years he covered both diagnosis and therapy with remarkably good results His diagnostic reports notable for their brevity were always written by his own hand; in X ray therapy he followed closely the technique of Coutard and though his dosage by modern standards was often low his results were good and he seldom distressed patients by his treatment.

In 1920 Robson was elected F R.C P and soon afterwards he became senior physician to the hospital In his capacity he took his share of the committee and administrative work and was a powerful figure both upon the hospital board of management and upon its medical board.

E. H. S writes: " Widely respected both by his medical colleagues and also by the thousands who had been his patients, Dr Robson will perhaps be even better remembered by his work for the nurses much of which was done in his latter years. Always a champion of the nursing profession and a sturdy advocate of better conditions, he was largely instrumental in introducing a scheme for the training as nurses of ex tuberculous patients at Creaton Sanatorium, an institution of which he was a founder member In his later years nothing gave Dr Robson greater satisfaction than the progress of the Creaton scheme whereby a number of ex tuberculous patients were able to receive their T A training and eventually hold posts at the sanatorium

Until recently a keen field sportsman he was a notable fly fisherman and had a wide knowledge of country lore. Indoors he was more than a match for most at the card table, enjoyed (and was always able to furnish) excellent port, and was an entertaining and amusing raconteur Courtly in his manner shrewd in his judgment, combining a quiet sense of humour with a natural dignity he was widely known and universally respected in Northampton and district.

Dr. Robson leaves a widow and a daughter

OTTO ROSENHEIM

Ph.D Würzburg F R.S.

The death of Otto Rosenheim at the age of 84 recalls the many notable contributions which he made to physiological chemistry or what we now call biochemistry

He was born in Germany and after taking his degree at Würzburg he worked for a time with Graebe in Geneva. About 1895 he came to this country where he worked for a time in Manchester His first official appointment was as research assistant in pharmacological chemistry to F W Tunnicliffe at King's College London in 1901 but he had been associated earlier with Tunnicliffe in an investigation on uric acid salts and the volumetric estimation of this acid They demonstrated that the so-called quadriurates of Sir William Roberts were mixtures or solid solutions of uric acid and biurates. They were also associated in an investigation (published in *The Lancet* in 1901) of the possibility that selenium might be a source of toxicity of beer the selenium arising from the sulphuric acid used in the preparation of the sugars used in fermentation At this time too they studied the influence of formaldehyde in nutrition and they showed that 1 in 5000 in milk and 1 in 9000 in food had no effect on healthy children Rosenheim used this finding in after years when on his annual trips to t Continent, North Africa, and Mediterranean islands, took with him a supply of milk to which formaldehy had been added

While working on the estimation of formaldehyde milk he came to the conclusion that the Adamkiew reaction for proteins, used by Hopkins and Cole for th isolation of tryptophan, was not due to glyoxylic acid the acetic acid used but to formaldehyde and traces other necessary substances in the sulphuric acid use When Tunnicliffe left King's College, Rosenheim join Halliburton and was appointed lecturer in 1904 and lat assistant professor of physiology With Locke he devis a new perfusion method for the mammalian heart, usi dextrose in oxygenated Ringer solution and followed th sugar metabolism. But his main interest at this time w the study of the constituents of nervous tissue In 19 he had worked out methods for the detection of choli in the breakdown of nervous tissues; he then embark on a bold undertaking with Mary Christine Tebb who he later married—the study of the chemistry of protag extracted from brain Liebreich Gamgee Blankenhor and later Cramer believed this substance to be a sing chemical entity but Thudichum had shown it to a mixture as early as 1874

Rosenheim and Miss Tebb revealed how cold aceto removed cholesterol from dried brain and how acetone then extracted protagon which, by further treatment with solvents could be separated into t substances—phosphorus-free phrenosin and kerasin, a phosphorus-containing residue containing sphin myelin Later Rosenheim improved the preparation these galactosides by extraction with pyridine and fin arrived at tentative structures for phrenosin and kera To lay the ghost of protagon had involved some extrem difficult and laborious manipulative chemistry and recognition of his contribution Rosenheim was in 1 elected F R.S

The putrefactive bases of putrid meat, a pop subject at the end of the first decade of this century, attracted his attention Dixon and Taylor claimed an extract of placenta had a pressor effect but Rosenh showed that if there was no putrefaction there wa pressor effect

He retired early giving up his readership of chemistry in the University of London in 1920 devoted himself to his rock garden But his restless of inquiry was not to be gainsaid and he intere himself in the pigments of edelweiss and young leaves

After a few years of retirement he came as a volun worker to the National Institute for Medical Rese at Hampstead and so began a second fruitful peri outstanding contributions to biochemistry With wife and Dudley and later with Dudley and Star he elucidated the distribution and constitution of natural bases of unknown function spermine spermidine present in many mammalian tissues

With Webster who had already worked out a valu technique for the testing of antirachitic materials rats, he began his important studies of vitamin Rosenheim, with Drummond and Coward had alre shown in 1925 that the precursor of the active subst found in foodstuffs on exposure to ultraviolet light known as vitamin D was in the sterol fraction He followed this up with Webster and was able to that the substance responsible for the effects the vitamin was ergosterol This culminated in hands at the Institute in the isolation of vitamin D

Rosenheim also made a notable contribution to knowledge of vitamin A With Drummond he showed the vitamin-content of cod liver oil was approxima proportional to the colour intensity produced by addi of arsenic trichloride This test, naturally unsuitabl pharmaceutical laboratories because of the arsenic modified by Carr and Price who used antimony trichl ide The commercial use of other fish-oils which Ro heim found to be richer in vitamin A than cod live began about this time

In 1932 the chemistry of the sterols and related acids had reached an impasse The structures ass to these substances looked improbable Diel obtained chrysene by selenium treatment d emphasised the X-ray findings in the study of sterol olecules Rosenheim and King then advanced a volutionary formula which has stood the test of time d has led to great advances in the chemistry of the rols, bile-acids, heart-poisons, sex hormones, and nstituents of the adrenals

Rosenheim was a remarkable man He had a phenomal memory, and having read widely and contemplaely he was a mine of reliable information on physioical chemistry He loved to get, as he said, to the ttom of things and spent hours in libraries tracing corded observations to their origin He was a meticuus worker in the laboratory and extremely methodical is sagacity, wisdom, and knowledge were available to e humblest inquirer, and no-one could wish to meet a ore helpful colleague

H K

Mr J F BALLARD, director of the Boston Medical brary, died on May 15, at the age of 76 He was conlting librarian to the Boston City Hospital, the Boston iversity School of Medicine, Tufts College Medical hool, Boston, and the Armed Forces Medical Library Washington In 1920 he visited Europe in the interest the China Board of the Rockefeller Foundation to v a medical library for the Peiping Union Medical llege in China During the sixty-two years he served librar he was active in building up its collections e med cal incunabula, which he began to assemble h the te Dr William Norton Bullard, have grown to r 800 books and medieval manuscripts In 1944 he plishe a scholarly catalogue of the collection and he wc ng on the preparation of a second volume, agin he catalogue up to 1955, at the time of his th e classification scheme which he devised has ed by many medical libraries

Diary of the Week

MAY 29 TO JUNE 4

day, 30th

ERSITY OF EDINBURGH
(Royal Infirmary, Edinburgh) Prof. S F Haines (Mayo Clinic) Thyroid Gland in Relationship to Neuromuscular Disease

sday, 31st

ERSITY COLLEGE, Gower Street W C 1
5 P M Prof G M Bull Physiology of Osmotic Diuresis and its Clinical Effects (Last Cushny lecture)
HT FLEMING INSTITUTE OF MICROBIOLOGY, St Mary s Hospital Medical School, Paddington W 2
M Prof A C Frazer Intestinal Function in Man
TUTE OF OBSTETRICS AND GYNÆCOLOGY
(Chelsea Hospital for Women Dovehouse Street S W 3) Mr F C Dwyer Lumbo sacral Backache
F OF DERMATOLOGY St John s Hospital, Lisle Street 2
M Dr J E M Wigley Alopecias

day, 1st June

UATE MEDICAL SCHOOL OF LONDON Ducane Road, W 12
Dr Imrich Friedmann Pathology of the Ear.
CIETY OF MEDICINE 1 Wimpole Street W 1
History of Medicine Sir Weldon Dalrymple ampneys Medical Students through the Ages
OF OBSTETRICS AND GYNÆCOLOGY
Hammersmith Hospital Ducane Road, W 12) Mr N F, rris Face and Brow Presentation
F DERMATOLOGY
Dr R W Riddell Tinea Capitis
RURGICAL SOCIETY OF EDINBURGH
(18, Nicolson Street) Dr W S Shearer Diagnostic ue of a Plain Film of the Abdomen

rsday, 2nd

L SOCIETY OF MEDICINE
M *United Services* Surgeon Rear Admiral S G Rainsford The *Thetis* Disaster
MAN GILLESPIE LECTURES
M (University New Buildings Teviot Place Edinburgh, 8) Dr John Gillies Induced Hypotension
L COLLEGE OF SURGEONS OF ENGLAND, Lincoln's Inn Fields, W C 2
M Mr Robert Roaf Natural History of Deformities as seen in India (Hunterian lecture)

F CAL SCHOOL OF LONDON
ur Porritt Carcinoma of the Breast
L MEDICAL SCHOOL, Paddington W 2
Such Analgesia and

Notes and News

WORLD HEALTH ASSEMBLY

THE eighth World Health Assembly is now being held in Mexico City under the presidency of Dr Ignacio Morones Prieto On May 12 Dr M G Candau, director general of W H O , presenting his annual report, declared that the two greatest challenges to the Organisation are the eradication of malaria and the use of atomic energy in medicine and public health Impressive results had been achieved in the fight against malaria As a result of energetic action by national administrations, often aided by W H O and other international and bilateral agencies, more than 230 million people had been either freed or protected from malaria "The future efforts to bring safety to over 370 million people still exposed to malaria must take into consideration the fact, now apparently established, that anopheline mosquitoes which transmit malaria may become resistant to insecticides" The anti malaria drive was now at the cross roads "If we continue present campaigns not only do we face the danger of local vectors developing resistance to insecticides, but we may also expect that governments would not continue indefinitely providing the funds necessary for these campaigns" The only course open was to abandon the old line of action aiming at malaria control and to concentrate on total eradication.

At a later meeting the Assembly elected the following six States to designate members to sit on the W H O Executive Board for a three year term Argentina Pakistan Philippines, Ecuador, Portugal, and Finland Members from the following States have retired Brazil, Canada, Denmark, Iran, New Zealand, and United Kingdom

Mr Milton Siegel, assistant director general in charge of the department of administration and finance, informed the programme and budget committee that the Organisation s financial position had improved as a result of progress in collecting the arrears of governments' contributions The arrears of active members were now only $400,000

Dr Andrija Stampar, president of the Yugoslav Academy of Sciences and Arts and president of the first World Health Assembly, was awarded the Léon Bernard foundation prize, in recognition of his "outstanding contribution and practical achievements in the field of social medicine"

THE ROYAL SOCIETY

THE annual conversazione of the Royal Society was held on May 19 As the custom is, those for whom the study of flora and fauna had lost part of its freshness could contemplate some newly evolved features of the universe—the atomic billiards that goes on in a nuclear reactor, for instance But, for all the exciting things that physics and chemistry and the rest had to show, it was the flora and fauna that made the most striking exhibits

The Marine Biological Association of the United Kingdom made their usual delightful contribution to the occasion, this time with a show of invertebrate animals from the tidal zone of the sea shore There were busy sea slaters, lethargic scorpion spider crabs, looking harmless enough for paddlers (but no one tested them), glinting jewel anemones, and a great deal more Near by, Dr W H. Thorpe, F R S , presented some of the results of his remarkable work on the analysis of bird song Like most animal sounds, bird songs are hard to describe in words, and even the most musical people are often at a loss to remember minute details of songs without the aid of a suitable notation Moreover, the naked ear can seldom catch the elaborate sound patterns of high frequency high speed, and rapid modulation Most of these difficulties have been overcome by new methods of recording the song is first recorded in the usual way and then played back into an instrument which analyses the pitch and strength of the successive notes The result is something like a musical score and an expert can read it without actually playing it This method has been used to uncover the singing habits of the chaffinch If a chaffinch is kept in a sound-proof aviary and never hears other birds holding forth in springtime, it can itself manage only a very simple and imperfect song But it produces a typical song if it can hear other chaffinches, even when they are a long way off and there are other birds making quite a clamour close at hand Most of this learning can be acquired in its first spring as a fledgling, before it has tried to sing itself, and it may be that it learns something before it comes out of the egg The song, once learnt, is bred for ever. A strange finding is that if several chaffinches are kept together in a sound-proof aviary they teach each other to sing a complex song but it is very different from that of a wild chaffinch. Dr Thorpe has noticed that birds in a particular region sing in a kind of local dialect but he did not say whether the accent of the birds near his department at Cambridge was highly thought of in the chaffinch world.

Dealing with rather larger animals Mr F C Fraser and Mr P E Purves, of the British Museum set out the evidence for the belief that, contrary to earlier views, whales can hear very well (but direct proof was lacking for there were no whales in Burlington House). The sound path is essentially the same as in terrestrial mammals, with precisely the modifications of structure of the tympanic membrane and ossicles required for receiving water-borne vibrations. Elsewhere Dr A J Cain and Mr I. C J Galbraith of Oxford illustrated the effect of geographical isolation on the evolution of birds in the Solomon Islands. Most of the land birds there came originally from New Guinea, and some of them now show clearly marked division into geographical races (or subspecies) in the various islands. Some birds, however, are still very much the same throughout the islands, and they are judged to be relative newcomers.

In the study of an animal often less agreeable than all these Dr A J Buller and Dr A C Dornhorst of St Thomas's Hospital, displayed on an oscillograph screen the features of sound transmission through the normal human chest. Sounds were passed via the mouth into the respiratory tree and there was a microphone on the chest wall which amplified and recorded the sound output on the cathode-ray tube. By this means it will be possible to analyse long recognised physical signs of chest disease more precisely than Laennec or any of his successors have hitherto been able to do. A very crowded exhibit was that of Dr R A Weale of the Institute of Ophthalmology who demonstrated a stereoscopic illusion—though not everyone could make the swinging pendulum behave as it should have done. On the other hand there were no illusions about Mr John Hadland's high-speed cinematography in the film presented by Dr D A McDonald of St. Bartholomew's Hospital. The traditional falling cat was as popular as ever in slow motion and Dr McDonald then explained how the injection of gas bubbles had made possible the filming of the blood flow in the arteries of experimental animals. The film's star was a stout-hearted young man who stood up to a punch in the eye so that his reactions could be demonstrated in detail.

University of Cambridge

On May 14 the following degrees were conferred:

M.B., B.Chir.—L M Barrett.
M.B.—J S Garfield.

*By proxy

University of Leeds

Dr G R Hargreaves has been appointed Nuffield professor of psychiatry and head of the department of psychiatry from Oct. 1.

Dr Hargreaves qualified in 1932 from University College Hospital. After holding resident posts at several London hospitals he was appointed assistant physician to the Tavistock Clinic. In 1940 and 1941 he served as command psychiatrist to Northern Command and in 1941 he was appointed psychiatric adviser to the War Office Directorate of Selection of Personnel. In 1942 the Directorate of Army Psychiatry was set up in the Army Medical Department of the War Office and Dr Hargreaves served as assistant director until 1945. On demobilisation he was appointed O.B.E. From 1945 to 1948 he held the post of chief medical officer to the Unilever Company. During this period he was also lecturer in mental hygiene at the London School of Hygiene and Tropical Medicine. Since the end of 1948 he has been chief of the mental health section of the World Health Organisation.

University of Wales

Dr Scott Thomson has been appointed part-time professor of bacteriology in the university at the Welsh National School of Medicine, Cardiff.

Dr Scott Thomson is director of the regional public-health laboratory of the Medical Research Council at Cardiff and has been lecturer in bacteriology in the medical school since 1946. He is also honorary consultant bacteriologist to the Cardiff Royal Infirmary and consultant adviser in bacteriology to the Welsh Regional Hospital Board. He graduated in medicine from the University of Edinburgh in 1933 and after holding a house-appointment at the Edinburgh City Isolation Hospital he took the D.P.H. Shortly before the war he was Lewis Cameron lecturer in bacteriology at the University. In 1940 he received the gold medal for his M.D. thesis and the same year he took the M.R.C.P.E. Later with the rank of major in the R.A.M.C. he served as bacteriologist of the penicillin research team set up by the War Office in 1943.

University of London

The following have passed the final examination for the degree of M.B., B.S.:

Honours.—H B Anstall (c), Guy's; Alison M Armstrong (a), Westminster; Kathleen M Barber (b), Roy. Free; D H Beigel (c), Bart's; P S Boulter (b, d, *University Medal*), Guy's; Eileen R Busby (d), Charing Cross; J L Dawson (a), King's College; Stanley Feldman (c), Westminster; Vorna P Firth (b), Guy's; R. C Hallowes (e), St Thomas's; B A L Hurn (d), Bart's; N. R. Kemp (a), Univ. Coll.; Peter McDonald (c), Bart's; Joyce M Pallett (c), Univ. Coll.; Hazel M Price (e), Roy. Free; K. P Robinson (c), Westminster; N E. Rust (c), St Mary's; Enid H Shaw (c), Roy. Free; R. A Stroud (c, e), Bart's; Averil M Walker (e), Univ. Coll.

(a) Distinguished in pathology and bacteriology. (b) distinguished in medicine. (c) distinguished in applied pharmacology and therapeutics. (d) distinguished in surgery. (e) distinguished in obstetrics and gynæcology.

Pass.—W N Agnas, Nazir Ahmed, Ann K Alstrop, R H Anderson, B G Andrews, J C Anthony, Davies Martino, N K Armstrong, D L Arnold, M. J Atwill, Malcolm Aylett, R. D Bailey, G C W Baker, R. T Barber, Winifred M Bartindale, B J Bartley, J F S Batson, J T R. Bavin, D G Belasco, Esther A Bence, J B Benwell, W M. Berry, R. W Bewicke, Rosemary H Blakeney, Enid M Blewett, P W Blower, A E. Blumenfeld, T A Bollston, J P Booth, P J Booth, G T K Boughey, T L Bowen, J B Bowes, Dorothy A Bowman, T A Boxall, T R Boyde, Jean O Boyston, Jean M Bradley, Derrick Bradshaw, J D Brennan, Susan M Broadbent, B J Brooks, J D Broome, Margaret E. Broughton, G C Brown, W A R Brown, N L Browne, Helen M B Buckell, R A Bugler, F H Burgess, D N Burke, R A Burke, Elizabeth A. Burn, M C D. Burton, Brenda J Butcher, I R Butler, C M. G Buttery, P H Byles, D A O Cairns, J J Camp, Gillian M. Cann, P J S Cannon, Sarah Capell, P J Carrie, R. P Carrington, E J Carter, Gerald Cattell, Anne Chandler, J A Chappel, R W Clark, Mary D Clarke, E G Clayton, B J Clayton Payne, Terry Coates, R G Congdon, M A Cooper, M D Coulter, M. J Cox, Hilary J Crawford, J N B Crawford, E. A P Croydon, G A. B Cunningham, I I Dalnow, Jean G M Dalrymple, J R. Dalton, J F Dand, Charles Jones, D F Dart, B I Davies, D B Davies, Gillian M. Davies, H T Davies, J G Davies, D J Davison, J T Davy, I M. Dawson, P H G Dawton, A G Day, D T F Deakin, Zaka Ud Dean, Peter Dening Smitherman, E. R Dingley, A D Dixon, Elaine C Donoghue, K E. Doran, Barry Dunn, Sheila M Eades, D G A Eadie, D A S Eddie, P C E. Edgecombe, C M. D Edmonds, Elizabeth B Edmond, J M. Elsby, J O Emery, J P S England, Helen Erskine-Murray, C A S Evans, T A Evans, L W S Eyears, Joan M. Feke, W J Fewel, T P Fidgeon, B H W Finlatson, Freda M. Fletcher, C. H Floyd, B H Fookes, D E. Ford, John Frampton, J J Fryatt, Roy Garton, D M. George, M C Gle, D J Gooding, Rodney Grahame, B H Grant, Philippa F Grant, A J Gray, R. C Green, R A Greig, D G C Griffith, M. N Griffith, Mary E. Habgood, Patricia Haig, Jennifer J Haley, Beryl M. L Hall, R C Hamber, R L Hargrove, I G Harries, W G H, Elizabeth A Harrison, D F Hawkins, M F Hawkins, Anne H, Rita Henryk Gutt, B D Hick, Rachel S L Hood, I S H, Judith C Howard, P J C. Howe, J G J Howell, A J G H, Elizabeth A Hudson, F M. Hull, G S Humphreys, J R Humphreys, A D F Hurdle, Rosalinde Hurley, Vera Ir, G R Isaac, Celia N James, Ivan Janota, L C Jolly, Bridget Jepson, Caroline M. Jones, R. B Jones, N L Jones, I M N Jo, P N Jones, D N Kennard, Barbara H. Kerley, R. M B K, A MacL Kingon, F N L Kircher, R. K. Knight, B A L, M H Lees, M. J Lefford, I F Levers, H J Lewis, Rhona Lind, H. M. Lipman, J H Lister, P M. Lloyd Jones, Patricia N Locken, J A London, G K. Lovatt, K L Lowings, F I Macada, B H McCombe, P B McCumish, R. I Macfarlane, J K. McKay, T H R. Macleod, Cordon Macpherson, Eric Mallett, J Mahjas, L J Marshall, Barbara L Marston, Annabel J M Mas, Dorothy M. Mayall, A J Membrey, I. S I Menzies, J S B Mey, Marion N Miles, C W Millar, J D Miller, N H Mills, Wendy I Mitchener, B K Montgomery, J C Moorshead, J A Moss, A I Munro, D M G Murphy, K W Murphy, G R. Myall, J M Nerney, Judith A Newmark, K H Nixon, F J O'Connell, Gabriel Okungbowa, I N Orhewere, J G H Owen, J H. Padel, Dolly I Pakshong, Ronald Palmer, J G Parkes, Mark I Parsons, S L. Payne, J F Pearson, G D Pegrum, T N Pemba, B I W Peeks, B M N Pitt, Jane Platnauer, Mary S Plumbly, G G Pollock, Robert Porteous, C N Poulter, R N Pringle, Jean M. Pritchard, M J Prophet, I O Pyle, J S Rahan, Elizabeth J Rashid, Victor Ratner, Avril I Reed, E L Rees, B F Reeves, Hilary Richards, Humphrey Richardson, Margaret N Riddell, Bruce Robertson, Jennifer M Robertson, Margaret R. Robinson, Doreen Rothman, Theodore Rowan, G H Ryder, C. R. Salmon, D E. Saunders, I M Scott, Ann I Screech, Jane M. Semmens, I N Sewell, C R Sexton, G F Shackleton, Joanna Sheldon, D A I Shephard, D H Short, H R Simons, I J G Smart, B S Smith, H J Smile, J T Snow, Michael Speight, J D Spink, Margaret F Staley, I I Stallabrass, Gillian M Stevens, J K Stewart, D M Stibbs, J M Stratton, T E. N Striven, Kathleen M Sumner, A D Surtees, Nora H Sutton, D N G Swan, Malcolm Swann, Hilary K C Swech, D M Symes, G W Tapper, R. E. Taylor, Leon I Tenby, J L Thirkettle, D K M. Thomas, J I Thomas, J M E. Thomas, L I Thomas, A F Thompson, J G Thomson, F I Thoresby, M H Thorp, Alsa M Thurgar, K. J Tilling, T J Tiplady, M B Todd, I J Tothill, Christine H Towner, Kathryn Tudor, Edward I G K Uden, Roger Unwin, G. E. Upton, J S Vassar, H B Vaughan, M D N Vicker, D N Wadge, Molly E. Wakely, H J Warrick, M V Wells, J E. N Wickham, Marie I Wigmore, Kenneth Willerspin, Roger William, Shirley F Willis, J S Withey, Margaret J Witt, A M Wood, N S Wright, A P Wyatt, H F Wyatt, J R. W Wynne, R. T Yip-Choy.

Sanderson Wells Lecture

Prof R A McCance F.R.S., will give the Sanderson Wells lecture on Tuesday, June 14 at 4.30 P.M. at the Middlesex Hospital, London, W 1. He is to speak on Old Thoughts and New Work on Breads White and Brown.

Royal College of Obstetricians and Gynæcologists

At a meeting of the council held on May 21, with Sir Arthur Gemmell, the president, in the chair, the following were elected to the council

As representatives of the fellows —J F Cunningham, Dublin T N A Jeffcoate Liverpool, H J Malkin, Nottingham J H Peel, London

As representatives of the members —J G Gallagher, Dublin, T L T Lewis London S D Loxton, Bristol

The following were admitted to the fellowship

D R Beaton, R K Bowes, J C Coetzee, Mary D Daley, L L Davey, Ian Donald A S Duncan, H R Duval Amy D Engineer, R Magnus Haines I MacG Jackson, D F Lawson A A Moon Roland Nattrass, J C Newbold, R. C Percival B H Shdares Hugh Stirling C W Taylor

The following were admitted to the membership

R. H O Bannerman David Barron H R C Benny D B Brown T I *Cope*, A C *Coulthard* K D *Drayton* W A W Dutton B A Gavourin, H S Gavourin, Tara Sankar Ghosh, A. R B Harston, Josephine M R Heber Beryl O Howie, P E Jeffery, Beryl M Joles, G W Korn, Wendy E Lewington J D Llywelyn Jones, Philippa M Ludlam J G Mathie Appuhandy Ariyaman Mahanama Mendis, David Methuen, Catherine H Mitchell, Nanda Gopal Mukherjee, Rathindra Nath Nag, R T Sears Harendra Bahadur Sinha, D H K Soltau A E M. Stevenson, O S Treisman, Yin Kai Tsao, J K Tully J A M V Belkum

Dr A M Sutherland was appointed William Blair Bell lecturer for 1955, and Prof Louis Hellman (New York) Green Armytage lecturer for 1956

University of Otago, New Zealand

Dr Harold Bourne has been appointed lecturer in psychiatry and junior physician at the medical school, Dunedin.

Faculty of Radiologists

The annual meeting of the faculty is to be held in Bristol on June 10 and 11 The subjects chosen for discussion are Ankylosing Spondylitis, Postgastrectomy Syndromes, Radio therapy of Rheumatic Diseases, and the Radiosensitive Bone Tumours Further details may be had from the secretary, 45, Lincoln's Inn Fields, W C 2

Medical Association for the Prevention of War

This association will hold a conference on Saturday, June 4, at 2 30 P M at 45, Russell Square, London, W C 1, on the *Medical Effects of Radioactivity* The speakers will include Dr George Discombe, Dr W R Doll, and Dr Richard Dobbs Dr Duncan Leys will be in the chair

General Practice Reform Association

The first annual general meeting of this association was held in London on May 21 with Dr Robert John, the president, in the chair Dr J J Segall, chairman of the executive committee, said that the association's purpose was to serve the real and long term interests of the profession as a whole and of the health services, with particular regard to general ctice, and consequently, because of present conditions, serve also the special interests of principals with medium small lists, assistants and other unestablished practitioners, the future generations of new doctors. The G P R.A ramme included the creation of regional health authorities ing about a unitary system of health services administra and organisation, the reduction, by stages, of the mum number of National Health Service patients per itioner from 5500 (the number at present permitted for ctitioner who employs another doctor as a full time ed assistant) eventually to 2000, the provision of health s in suitable localities, the replacement of the assistant system by a satisfactory general practitioner training e, with the trainee employed by an appropriate rity, and the restoration to N.H S patients of full freedom of change of doctor The G P.R A did not wish to rival the older medical organisations, and it was hoped that stronger relations with them would develop Dr L Russell, deputy chairman of the executive committee, speaking of the Minister of Health's committee on medical man power, expressed a hope that the estimates of the number of general practitioners required would be based on a maximum of 2000 N H S patients per practitioner A resolution was passed urging the Ministry of Health, the Medical Practices Committee, and the General Medical Services Committee (or counterparts in Scotland) to take steps to obtain consideration for unestablished practitioners of executive council practice vacancies, including on and mainte of a central register of the appointn

British Association of Pædiatric Surgeons

The association will hold its annual meeting in Glasgow from June 15 to 17, under the presidency of Mr Matthew White Further particulars may be had from Mr W M Dennison, the Royal Hospital for Sick Children Glasgow, C.3.

Hospital Pharmacists

The salaries of pharmacists working in hospitals or health centres have been increased, from April 1, by sums ranging from £50 to £125 a year according to grade and length of service

Prison Medical Service

The annual conference of prison medical officers and psychologists was held at the Home Office on May 20 Dr H K Snell, director of medical services of the Prison Commission, was in the chair The speakers included Dr J D W Pearce, Dr I A Angus, and Dr C F T Saville

Ciba Foundation

On Wednesday, June 15, at 5 P M, at 26, Portland Place, London, W 1, Dr H Olivecrona, professor of neurosurgery at the Karolinska Institute, Stockholm, will give the seventh Ciba Foundation lecture He is to speak on Hypophysectomy in Diabetes

British Orthopædic Association's Belgian Visit

On April 22 and 23 Prof Bryan McFarland the presid and some twenty members of this association attended the spring meeting of the Société Belge d'Orthopédie et de Chirurgie de l'Appareil Moteur at Brussels at the invitation of the president, Dr Robert Soeur A report on the functional results of arthroses was presented by Dr de Racker

The 48-hour Week in the N H S

A conference of the National Union of Public Employees, reported in the *Times* of May 24, instructed the union's executive council to press for a 44-hour week for ancillary staff of the National Health Service The present 48-hour week was held responsible for the serious drift of labour from the service, the failure to attract new entrants, and "widespread discontent now existing among ancillary st

Rockefeller Grants

The Rockefeller Foundation has made a five year grant of £15,000 for a new department of occupational health at the London School of Hygiene and Tropical Medicine It has also made a £12,500 grant for a three-year period to assist research in the department of physics at King's College Hospital under Prof J T Randall, on the structure of nucleic acid

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CORRIGENDUM *Beneventi's Retropubic Prostatectomy* —The price of this book was given incorrectly in our review (May 21) It is

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Appointments

CHUDECKI BRONISLAW M B Cracow, D.M.R T asst radiotherapist Exeter clinical area

LEWIN, W S M S Lond, F R.C.S consultant neurosurgeon United Cambridge Hospitals and for duties in East Anglia R H B (To take up duties in 1956)

MORROW W F K, M B Belf, D A anæsthetist Banbridge and Dromore and Southdown H.M.C s, Northern Ireland Hospitals Authority

* SALFIELD, D J, M.D Düsseldorf, D I M whole time consultant children's psychiatrist, Sheffield R.H B., for Derbyshire.

SLEIGH, JOHN, M B Aberd, D P H deputy M O H deputy princi school M O, and deputy port M O Newport Monmouthshire

Appointed Factory Doctors

REEVES, G W D, M R C.S Breage, Cornwall

SKINNER DAVID, M B Aberd Burnley South Lancaster

Colonial Appointments

ALDERDICE, A. A M B Sydney M R.C I senior specialist Uganda

BAIRD J C M B Glasg M O, northern region Nigeria

BELL, W L H L M.R C.S health officer, Malaya

BENNETT, L B G, M B Camb surgeon, St. Lucia

BOASE, A J, O B E, F R C S, D O.M.S senior specialist Uga

COELLO, A J, L.M.S Barcelona D P H M O (grade A), physician Trinidad

GENTLE G H K M R C.S, D T.M & H superintending M A (specialist) V D division, Trinidad

HAMBLETT E P M B Brist D C H district M O Dominica

HARRIES, J R, M D Lond M R C.P, D C.H, D T.M & H medical specialist Kenya

MAURER, S P, M B N U I health officer Malaya

O GARRA MARGARET M R. M B Lond district M.O, Antigua

TROWELL, H C O B E M D Lond, F R.C I senior specialist Uganda

INTERPRETATION OF INJURIES IN THE COMET AIRCRAFT DISASTERS

AN EXPERIMENTAL APPROACH

J A Armstrong
M.Sc., M B Lond
FLIGHT LIEUTENANT
R.A.F MEDICAL BRANCH

D I Fryer
B.Sc M B Lond
FLIGHT LIEUTENANT
R.A.F MEDICAL BRANCH

W K Stewart
C.B E., A.F C B.Sc., M B Glasg
GROUP CAPTAIN R.A.F MEDICAL BRANCH
R.A.F INSTITUTE OF AVIATION MEDICINE, FARNBOROUGH
HANTS

Sir Harold E Whittingham
K.C.B., K.B E., LL.D Glasg F.R C.P F R C S E
DIRECTOR OF MEDICAL SERVICES BRITISH OVERSEAS AIRWAYS
CORPORATION

On the morning of Jan 10 1954 the Comet air liner ALYP took off from Rome airport en route for London with 35 people on board About twenty five minutes later a sound like an explosion was heard and the aircraft in pieces crashed into the sea near Elba There were no survivors but within about four hours 15 bodies were recovered from the sea in an area some $1^1/_4$ miles in diameter All but 1 of the bodies were floating face downwards when found 5 were naked or almost so retained only a few garments and 6 were still well clothed 11 of these people had almost certainly been in the rear part of the main cabin at the time of the disaster and those who had occupied the back seats were more [illegible] up than those from more [illegible] lies were taken to Elba and between Jan 12 and Jan 14 all but 1 were subjected to detailed necropsy by Prof A Fornari of Pisa

On the evening of April 8 another Comet air liner (G-ALYY) disappeared on a routine flight from Rome to Cairo with 21 people on board The following evening 5 bodies were found floating on the sea near Naples and picked up by H M S *Eagle* As on the previous occasion all but 1 floated face downwards. It is estimated that they were in the water for about twenty two hours including most of the daylight period of April 9 A 6th body was washed ashore ten days later at Paola Of these bodies 1 was *almost fully clothed* 1 was scantily clad, and the other 4 were practically naked All were passengers from the rear part of the main cabin the front seats had been unoccupied The bodies retaining most clothing had again occupied the rearmost seats 5 of the bodies were subjected to necropsy in England by Dr Donald Teare on April 12 and 13 and the remains found at Paola were examined by the Italian authorities

Many intricate investigations spread over about nine months were undertaken at the Royal Aircraft Establishment and elsewhere to find out the exact nature and basic cause of the disasters and hence to devise measures to prevent their recurrence In this work the medical evidence assumed immediate importance owing to the absence, for some considerable time of wreckage which would facilitate reconstruction of the Elba accident Owing to the depth of the sea off Naples salvage operations were impossible and no significant wreckage was forthcoming consequently the medical evidence in this instance was of particular importance in so far as it showed that both accidents had essentially the same effects on the passengers.

The necropsy findings are of interest quite apart from their place in the inquiry owing to their somewhat unusual nature and the unique circumstances in which the injuries were sustained In modern air liners it is necessary to pressurise the cabin to protect passengers from the hazards of anoxia and decompression sickness at high altitude At the time of the disasters both Comets had reached an altitude of about 30 000 ft during the initial climb At this height the air pressure inside the cabin is about 7 5 lb per sq inch (388 mm Hg) above that prevailing outside In recent years there has been much speculation about the possible consequences of a sudden structural failure causing very rapid ("explosive") decompression In particular damage to the lungs has been feared owing to the rapid expansion of intrapulmonary gas (Armstrong 1936 Lovelace and Gagge 1946 Fulton 1948) Clearly such a possibility had to be considered in the Comet victims for break up of the fuselage at 30 000 ft, whatever the cause would be accompanied by rapid decompression Nevertheless any lesions due directly to decompression would be associated almost inevitably with others due to violent impact with parts of the aircraft or its furnishings Another possibility was blast injury due to some kind of explosion Moreover all injuries inflicted in the aircraft might well have been complicated by the effects of a free fall from high altitude by impact with the sea and by effects of exposure while floating on the sea in the vicinity of the crash

The medical inquiry had three *main* objectives (1) to record all lesions found at necropsy (2) to identify the cause of death, and (3) to ascertain in accordance with these facts the probable nature and sequence of traumatic events We do not give a full description of the necropsy findings because a brief summary of the outstanding features will serve as adequate introduction to the description of the necessary research with which we were primarily concerned

The major injuries in all the bodies from both accidents were remarkably uniform All but 5 of the 19 bodies examined had ante mortem fractures of the skull and 15 had similar injuries to the thoracic cage mostly of exceptional severity Spinal fractures and costo-vertebral dislocations were common Limb fractures found in 13 cases, were identified as predominantly post mortem Grave internal injuries were present in all the bodies even in those with little external injury Thus, hæmothorax *of* 0 3–2 0 litres was present in 10 *cases* and the lungs were severely damaged in all 19 In no case however was there evidence of drowning The heart was ruptured in 4 bodies and the great vessels were torn in 13 *Intra abdominal injuries were rather less common* but hæmoperitoneum (up to 1 litre) was present in 14 cases and hepatic laceration or pulping was invariable Only 5 cases had tears of the spleen In addition areas of altered skin were observed in 14 of the Elba victims and in 4 from Naples in the former they were likened to burns or scalds whereas in the latter the change was apparently in pigmentation

Analysis of these findings led to the conclusion that three aspects of the problem needed special investigation if the medical evidence was to be of positive value in reconstruction of the accidents (1) the *ætiology of the pulmonary lesions* (2) *the cause of the skin lesions* and (3) the feasibility of distinguishing between ante mortem and immediately post mortem injuries with special reference to the effects of violent contusive trauma The last point is important in any attempt [illegible] time sequence

Pulmonary Lesions

PATHOLOGY

Severe injury to the lungs was an invariable finding The predominant *naked-eye lesions* were [illegible] bruising laceration pulping and areas of [illegible] with subpleural bullæ

Irregular *lacerations of various depths were* [illegible] the lungs *in most cases* They were [illegible] the lower lobes, chiefly on the diaphragmatic surfaces, and sometimes extended into areas of complete pulping Only occasionally could the lacerations be attributed to penetration by fractured ribs, they were prominent in the 2 cases in which the thoracic cage was intact The margins of the tears were clearly hæmorrhagic in all but 2 cases These 2 bodies (numbers 14 and 15 from Elba) also differed from the others in showing no hæmothorax It seems likely that the pulmonary splits in these 2 cases occurred after the circulation had ceased

Subpleural hæmorrhages and congestion were present to some extent in all instances, giving a mottled appearance to the surface Slices showed that the hæmorrhagic zones often extended deeply into the lung, and that hæmorrhages were scattered throughout the pulmonary parenchyma In no case did the subpleural hæmorrhages present a definite linear pattern of "rib-markings" In contrast with the dark areas of congestion and bruising, other parts of the lungs seemed unusually pallid, bloodless, and expanded Tense subpleural bullæ occurred in these areas, especially in the upper lobes

Portions of the lungs from 18 bodies were examined microscopically at Farnborough The Elba specimens had been fixed in 10% *formalin, and those from Naples in* Zenker-formalin Paraffin sections were stained for general histology with Ehrlich's hæmatoxylin and eosin, and by the Masson trichrome method Wilder's silver chnique was used for the demonstration of reticular res, and mucus was identified by the periodic acid-iff reaction Other pieces of lung tissue from each y were embedded in gelatin by the procedure des-d by Baker (1946), frozen sections 15–25 μ thick stained for neutral fat with alcoholic solutions of n III and IV, or Fettrot 7B (Pearse 1954)

tensive disorganisation of the finer structure of the was found in every case The outstanding lesions traumatic emphysema, hæmorrhage, vascular gement, and fat embolism

most striking feature in the sections was the ce of adjacent large areas of emphysema and rhagic consolidation So far as could be deduced he samples taken for histology, these features were but not uniformly distributed throughout the in places the emphysema was massive, notably parts of the upper lobes where macroscopic bullæ en observed at necropsy The emphysema was traumatic (figs 1 and 2) In the affected parts lls of alveoli, alveolar ducts, and respiratory and al bronchioles were torn, with consequent formation of irregular spaces varying greatly in size, the largest being about $^{1}/_{4}$ inch in diameter Remnants of the torn alveolar walls projected into the spaces, and in sections stained by Wilder's method reticular fibres were seen protruding from the torn edges As might be expected, such changes were not restricted to the pre-existing air spaces of the lung but were accompanied by interstitial emphysema due to the formation of direct communication between the air spaces and the connective tissues of the bronchovascular planes and interlobular septa The subpleural bullæ were of this type, evidently *caused by escape of air into the deeper layers* of the visceral pleura (fig 1) The severity and distribution of traumatic emphysema bore some relation to the normal anatomical pattern of pulmonary lobules Thus, distended areas with great destruction of lung parenchyma were commonly adjacent to areas of collapse or of relatively normal lung and separated from them only by interlobular septa Nevertheless collapse, hæmorrhage consolidation, and emphysema could, in places, be seen side by side in the same lobule In some cases the bronchi and bronchioles contained plugs of material including epithelial cell debris, a few red blood cells, and matter, presumably mucus, which stained with periodic acid Schiff reagent (fig 3)

In all but 2 bodies the blood vessels and lymphatics of the lungs were congested There was gross intra-

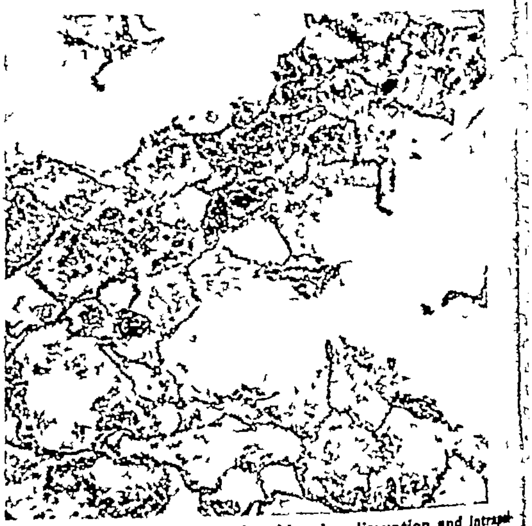
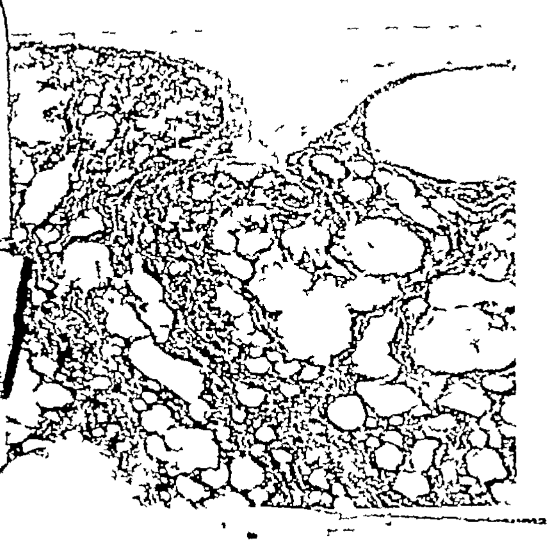


Fig 2—Naples accident body C. Alveolar disruption and intrapulmonary hæmorrhage in upper lobe of right lung (Hæmatoxylin and eosin ×52.)

pulmonary hæmorrhage, but this varied considerably from one part of the lung to another Much of the blood seemed to have come from the innumerable disrupted capillaries, but arterioles and even small arteries were occasionally found opening directly into the air spaces Over large areas the alveoli were completely packed with blood, giving a condition of hæmorrhagic consolidation or hepatisation, and in places the pleura was separated from the underlying parenchyma by extravasated blood Some of the alveoli and emphysematous spaces also contained what appeared to be œdema fluid and amorphous debris Bodies 14 and 15 from Elba, however, showed little evidence of intrapulmonary exudation or bleeding, although there were severe traumatic emphysema

In several specimens there were early signs of post-mortem autolysis and putrefaction due to bacteria which could be seen in the sections, particularly in regions of gross hæmorrhage In these cases it was not difficult to distinguish between smooth walled spherical spaces produced by the action of gas forming organisms the irregular cavities of traumatic emphysema



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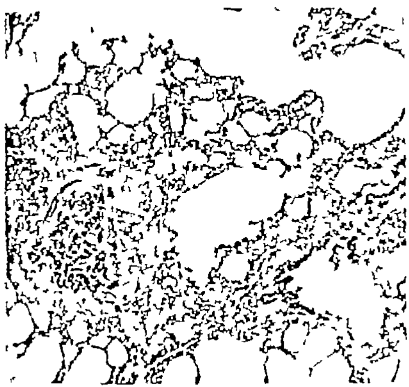

Fig. 3—Elba accident: body 4. Bronchiole occluded by cell debris and mucus, and another partially denuded of epithelium. (Hæmatoxylin and eosin. ×52.)

The frozen sections revealed pulmonary fat embolism (fig 4) in 12 bodies. The amount was small in most cases but in 3 (2 from Elba and 1 from Naples) it was considerable. The quantity of intravascular fat observed in the few frozen sections examined from each case does not, of course, necessarily indicate the total embolic fat-content of the lungs and must therefore be interpreted with due reserve. However, the mere presence of fat-embolism is of interest in so far as it might help to determine the sequence of injuries. It is unlikely that the fat originated within the lungs. Ante-mortem fractures are usually assumed to be the source of pulmonary fat-embolism but this is not always so (Robb-Smith 1941). All 12 cases with which we are now concerned had fractures with local ante-mortem characteristics, but 1 case showing considerable fat-embolism was also 1 of the only 2 bodies with an intact thoracic cage, having ante-mortem fractures only of the skull.

The fat-embolism suggests that the pulmonary circulation was maintained for a finite time after the cranial or thoracic fractures were sustained. In 5 of these bodies all the vessels forming the vascular peduncle of the heart (including the pulmonary arteries) were either extensively torn or completely severed. We therefore suggest that these injuries to the great vessels occurred a sufficient time after the fractures for pulmonary fat-embolism to develop, and that during this time the intrapulmonary vascular bed was also largely intact.

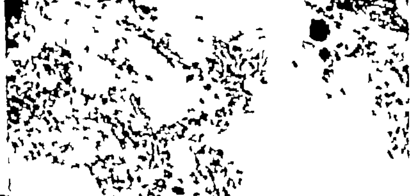

Fig. 4—Naples accident: body C. Pulmonary fat-embolism. (Sudan III and IV. ×200.)

PATHOGENESIS

Lung injuries of a similar type have been described before, clinically or under experimental conditions, in at least three different situations: (1) in exposure to the effects of explosive blast; (2) as a result of very rapid ("explosive") decompression; and (3) as a result of certain severe forms of body impact and abrupt deceleration. Initially it seemed reasonable to suppose that any or all of these conditions might have prevailed at some time during the course of events associated with sudden structural failure at high altitude of a pressurised aircraft such as the Comet. It was therefore necessary to investigate each of these possibilities in some detail.

Blast Injury

The pathological and physiological effects of air blast from gunfire or detonation of high explosive have been observed in animals under experimental conditions (Hooker 1924, Zuckerman 1940, 1941).

Rabbits, mice, and other species killed outright showed no external injuries, but nearly all had blood or blood-stained froth in the upper respiratory passages. The outstanding lesions in all specimens killed or injured were alveolar disruption and massive pulmonary hæmorrhage, amounting in places to complete hepatisation. The injurious effects of blast diminished with increasing distance of the animals from the explosion. Hæmorrhages under the visceral pleura tended to assume a linear pattern of distribution, forming the so-called "rib markings." Animals exposed to underwater blast developed essentially the same pulmonary pathology (Williams 1942, Cameron et al. 1942). More recently Greaves et al. (1943) and Clemedson and Granström (1950) have shown that the subpleural hæmorrhagic bands do not correspond to the ribs but lie beneath the intercostal spaces.

Cases of death or injury in man due to air blast have been reported (Hadfield et al. 1940, O'Reilly and Gloyne 1941, Osborn 1941, Wilson and Tunbridge 1943). Lung damage, termed "pulmonary concussion," was similar to that described by Zuckerman (1940). Hæmorrhagic "rib markings" were the rule in children, just as in the experiments on animals, but in many adults such markings were not found. Elasticity of the chest wall may be a determining factor in this matter. Nearly all the fatalities and most of those severely injured had blood or bloodstained froth issuing from nose and mouth. In actual bomb incidents, however, severe pulmonary concussion was usually accompanied by additional evidence of the explosion, such as skin wounds caused by flying missiles (including bomb fragments) or burns from the fireball.

Very little is known for certain about the precise mechanism of pulmonary concussion, beyond the fact that it is an impact phenomenon resulting from impingement of the positive pressure component of the blast wave on the body wall (Zuckerman 1940). Three ætiological factors have been suggested: (1) direct deformation of the lung tissues (Osborn 1941); (2) differential acceleration of the various structural elements of the thorax (Clemedson and Granström 1950); and (3) transmission of a shock wave through the tissues (Williams 1942). It may not be a question of which theory is correct, but how much each factor contributes in any particular instance. Presumably the same factors operate whenever this type of lung injury, localised or diffuse, results from any form of non-penetrating blow to the chest wall. Penney and Bickley (1943), analysing unpublished numerical data on blast injury provided by Zuckerman, proposed that the lungs of any animal, including man, severely injured if the chest walls are flung inw

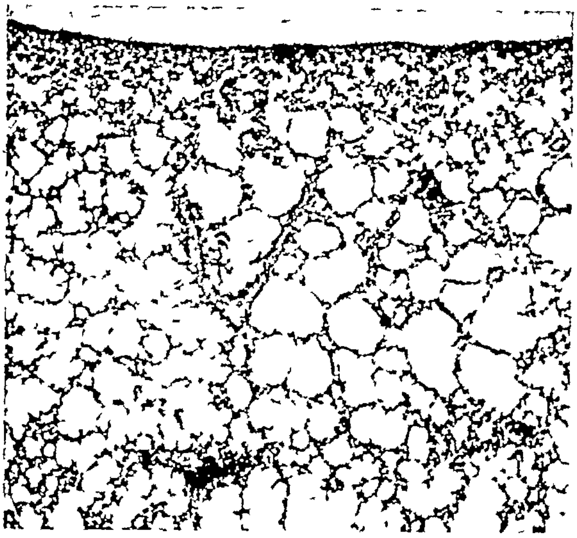

Fig 5—Guineapig lung after explosive decompression from 0 to 35,000 ft. in 0 006 sec. (Hæmatoxylin and eosin ×40)

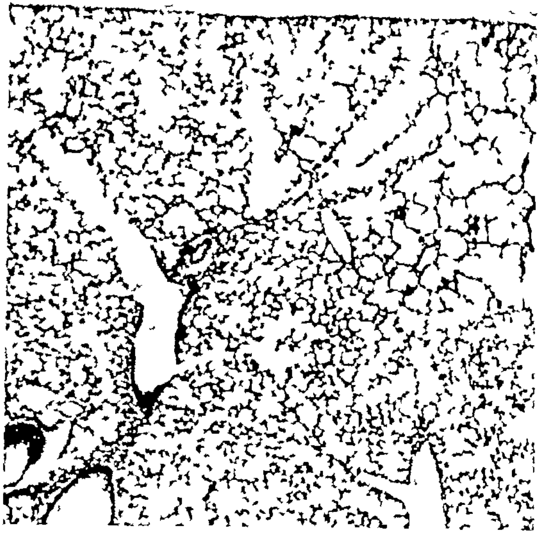

Fig 6—Lung showing normal appearance in control guineapig killed with ether (Hæmatoxylin and eosin ×40)

such acceleration that they acquire a velocity of 20 metres per sec in half a millisecond or less

Analysis of the necropsy findings in the Comet victims has led us to conclude that the pulmonary lesions were in all probability not caused by an explosion, the reasons being as follows

(1) In none of the bodies recovered (including that of a child aged 10 years) did the subpleural hæmorrhages show a pattern of "rib markings"

(2) The lungs of all had much the same appearance, whereas in blast a significant variation in the degree of injury might be expected, people seated near the source being most severely affected

(3) In no case was blood or froth present in the nose, mouth, or elsewhere in the upper respiratory passages

(4) None of the bodies had skin lesions attributable to peppering with metallic fragments or other missiles

(5) None had burns such as are caused by naked flame

Incidentally, it may be noted that examination of the wreckage recovered from the sea bed off Elba led structural experts to conclude that there was no evidence of a bomb explosion or of any fire inside the cabin of the aircraft

Explosive Decompression

The possible dangers of failure of a pressurised cabin at high altitude have been studied by physiologists since they were first consulted by aircraft designers about 20 years ago, when commercial high-altitude flight was first advocated Initial fears were soon allayed by experiments (Heim 1938, Garsaux et al 1939, Bergeret and Giordan 1939) Military applications of high altitude flight led to an intensification of research, and experiments made on man in this country (Flying Personnel Research Committee 1942), the United States (Sweeney 1944, Hitchcock 1953), and in Germany (Benzinger 1950) showed that man can tolerate extremely rapid decompression without ill effect After the war, when civil pressurised transport aircraft became a practical proposition, there was an urgent need for a clear exposition of the limits of human tolerance, so that an aircraft designer could estimate the risk to passengers from failure of a given area (e g , a door, a window, or a hatch) at a known pressure differential A formula, based on an interpretation of some experimental data, was proposed by Lovelace and Gagge (1946) Its validity has recently been challenged (Fryer 1953, Violette 1954) and an alternative means of assessment devised (Violette 1954)

O[illegible] ledge of the pathological sequelæ of explosive d[illegible] is based upon two sets of data (1) the results of very numerous experiments on animals (Eggleton et al 1945, Hitchcock 1953, Rotondo 1953), and (2) a little information on the injurious effects of explosive decompression on man In animals it has proved very difficult to cause death or even symptoms, provided that prolonged anoxia has been avoided For example, of 19 dogs decompressed from 10,000 to 50,000 ft (a pressure differential of 8 4 lb per sq inch) in 0 012 sec none developed any symptoms, although small areas of pulmonary hæmorrhage could be detected if the animals were sacrificed soon after the experiment (Edelmann et al 1946) Of the lesions described by various workers, the most predominant has been scattered pulmonary hæmorrhages, often accompanied by areas of collapse Emphysema has also been described, and "rib markings" were noted by Rotondo (1953) In none of these experiments was the injury comparable in severity with that found in the Comet victims, and some of it at least can be attributed to the methods of sacrifice used after recompression Cole et al (1953) report more extensive lesions, but in these experiments the picture was undoubtedly complicated by exposure to atmospheric pressures below that of the vapour pressure of water at body temperature—i e , when the tissue fluids "boil" The lung damage in these circumstances exceeded anything previously observed in experimental explosive decompression

In experiments at Farnborough 10 adult guineapigs were decompressed from 0 to 35,000 ft (11 2 lb per sq inch) in 0 006 sec and then immediately brought to ground level The guineapigs appeared mildly startled by the experience but showed no signs of respiratory distress and behaved quite normally during and after recompression They were then killed with ether Outwardly the lungs appeared congested in most specimens, but in 1 there were distinct hæmorrhagic "rib markings" Microscopically there was congestive atelectasis interspersed with areas of alveolar distension (fig 5), but rupture of alveoli was uncommon, and hæmorrhages were few and widely scattered

The lung lesions found in animals may be explained (at least in part) by the development of high pressure differences between the lungs and the atmosphere, with resulting overdistension of the thorax if the rate of environmental decompression is greater than the maximal rate at which the lungs can void their contents through the trachea

The ill effects noted in man are few Two cases of pneumomediastinum (Vavala 1954) and 1 of death from rupture of the lungs and massive air embolism (Benson

1953) have occurred in the course of many hundreds of explosive decompressions under identical conditions during routine altitude tests in the United States Benzinger described two incidents in Germany in which air-embolism is thought to have occurred during voluntary breath holding in the course of explosive decompression. These phenomena are known complications of the decompression incurred during submarine escape if the glottis is closed (Polak and Adams 1932) Pneumomediastinum may similarly result from pulmonary alveolar rupture allowing air to track interstitially via the hilum to the mediastinal tissues It therefore appears that closure of the glottis might render serious or fatal an otherwise harmless decompression No pulmonary lesions resembling those found in the animals have ever been observed in man after explosive decompression

It is seen, then that the widespread pulmonary lesions of the Comet victims might be attributable to explosive decompression if the conditions were such that the violence of the decompression exceeded the limits of human tolerance by a wide margin On the basis of the formulæ derived by Lovelace and Gagge (1946) the possible borderline between safety and "uncertainty" would correspond in the case of the Comet flying at 30 000 ft to the instantaneous breaching of the cabin wall by removal of an area of 154 sq ft In such circumstances the decompression would take 0 062 sec However, the more recent interpretation by Violette (1954) suggests that injury would result only if an area of more than 290 sq ft was lost, giving a decompression time of 0 032 sec In fact the expert examination of the wreckage of the Comet aircraft G ALYP suggests most strongly that the primary failure involved the loss of a maximal area of 162 sq ft, and that the splitting process which resulted in this failure took a finite time, which prolonged the decompression well beyond the calculated 0 059 sec in the case of instantaneous disruption In Sweeney s experiments decompression from 8000 to 35 000 ft (7 5 lb per sq inch) in 0 09 sec proved completely innocuous for 15 young adults and 160 decompressions from 10 200 to 35 000 ft (6 55 lb per sq inch) in 0 075 sec caused no ill effects

From such considerations it seems most unlikely that all the occupants of the aircraft should have sustained severe pulmonary injury from the primary effects of explosive decompression in the circumstances suggested by investigation of the wreckage In addition it is noteworthy that there was no evidence in either accident of gross air-embolism or of mediastinal emphysema

A second and probably more relevant result of explosive decompression is the expulsive effect of the air released when a large pressure-cabin fails This is discussed more fully below

Impact

Fatal falls from a great height to the ground are not uncommon it is well known that in such cases there may be extensive internal injuries even when there are few external signs of trauma (Gosselin 1847 Moritz 1954) The destructive *forces involved are presumably much* the same as when the body is struck by a blunt moving object or by a blast wave the only difference appears to be that here the effects are decelerative rather than accelerative An important contribution on this subject was made by American workers investigating the rôle of deceleration in the genesis of injuries in military aircraft accidents Hass (1944) referred to 21 cases in which at necropsy laceration hæmorrhage and traumatic emphysema in the lungs were found there was also tearing of the heart and aorta laceration of the liver spleen and ileum and much free blood in the body cavities Similar lesions were produced experimentally in animals by very abrupt deceleration (Rushmer et al 1946 Rushmer and Hass 1940) The injuries were attributed partly to direct deformation and partly to differential deceleration of the tissues To these should be added the possibility of shock wave propagation

Since the Comet G ALYP is known to have broken up at high altitude there is reason to suppose that the occupants of this machine were twice subjected to decelerative forces; inside the aircraft at the time of initial failure and on impact with the sea The altitude at which they left the fuselage is a matter for speculation, but a free fall of 2000 ft is adequate for a human body to attain its terminal velocity of about 160 ft per sec It is important to know whether the internal injuries could have been caused partly or entirely by impact with the sea The observations of Merkel (1926) and Ziemke (1928) on falls into water from heights of up to 150 ft suggest that this is most probable and that death may take place without signs of drowning Very little is known about these matters, and it has been necessary to investigate them experimentally in guineapigs

EXPERIMENTS ON GUINEAPIGS

Rationale of Experiments

The forces generated by impact of a rigid sphere with a water surface were studied by Richardson (1948) and from his results it has been possible to deduce the approximate incident velocity necessary in any given species to produce the inward movement of the chest wall specified by Penney and Bickley (1943) as critical for the production of blast injury in the lungs Details of the mathematical method have been published separately (Stewart et al 1955) and the calculations showed that the critical incident velocity for the mouse would be about 118 ft. per sec for the guineapig 90 ft per sec and for man 94 ft per sec

Material and Methods

A vertical catapult was constructed for projecting anæsthetised or dead guineapigs at known velocity into a tank of water 5 ft deep The catapult consisted of a small metal carrier moving vertically on a tubular steel upright and powered by six strong rubber cords The carrier could be raised to the desired height with a block and tackle and was fired by a manually operated release The guineapig was lightly secured by strips of adhesive paper to the under surface of the carrier so that when the latter was arrested at the lower limit of its excursion the guineapig was projected belly first about $2^1/_2$ ft through the air before hitting the water The attitude on impact was checked by cinephotography which revealed that the body usually rotated a little in the air The incident velocity was measured in two ways by high speed cinephotography and by an electrical method using a slide wire connected to the carrier These gave almost identical results

The guineapigs were either male or female albinos weighing 300–400 g 10 guineapigs were projected into the water at velocities between 66 and 117 ft per sec 6 were anæsthetised with ether and the 4 others received an overdose of ether so that all respiratory movements had ceased 10 minutes before the experiment Preliminary experiments showed that many anæsthetics and commonly used methods of killing animals in the laboratory may by themselves cause a remarkable degree of hæmorrhage or vascular congestion in guineapig lungs Coal gas was particularly injurious sometimes even producing rib markings Several control specimens killed with ether however, showed no evidence of pulmonary damage on naked-eye and microscopical examination (fig 6)

In 3 of the anæsthetised guineapigs subcutaneous electrocardiographic electrodes were inserted into the right forelimb and both hindlimbs before they were fixed to the carrier After the catapult was fired each animal was left in the water for one to two minutes Anteroposterior and lateral radiographs of the whole body were taken and the guineapig was then dissected Particular attention was paid to the condition of the thoracic and

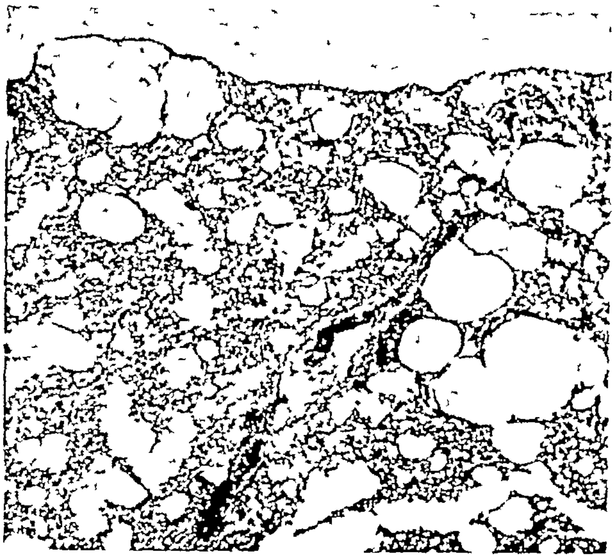

Fig 7—Lung from anæsthetised guineapig projected into water at 117 ft. per sec., showing intrapulmonary hæmorrhage and traumatic emphysema. Compare with figs. 1 and 2 (Hæmatoxylin and eosin × 40)

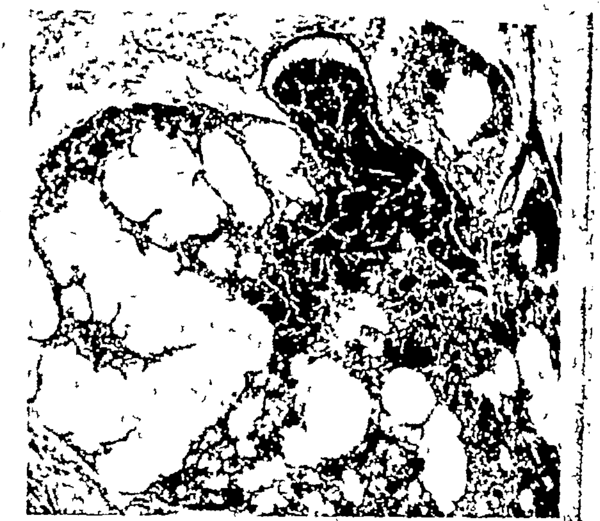

Fig 8—Lung from an anæsthetised guineapig projected into water at 107 ft. per sec. Note large bronchial plug composed mainly of stripped epithelium (Hæmatoxylin and eosin × 68)

abdominal contents The trachea was first ligated, the chest was opened, and the heart and lungs were examined in situ. In some guineapigs these organs were removed, photographed, and fixed by submersion in Zenker-formalin In others the hilum of the right lung was ligated, the left atrium opened, and the left lung then perfused through the pulmonary artery, at a pressure of 20 mm Hg, with physiological saline solution followed by Zenker-formalin at 37°C, next, the thoracic contents were removed in toto and fixed by submersion in Zenker-formalin for a further twenty-four hours In every case paraffin sections were prepared from each lobe of both lungs, and stained by the same techniques as used for the human necropsy material

1 other guineapig was projected at a velocity of 100 ft per sec into a large pile of cotton-wool instead of into water, this was done as a control test to determine what effects, if any, might be attributable to the acceleration of the catapult

Results

On recovery from the water all the guineapigs showed little external sign of injury, but all of the anæsthetised guineapigs were now dead Most had some body flattening, 4 had bruises on the inner sides of the limbs or under the mandible, 1 had lost most of the hair from a large area on the front of the thorax, and 4 had palpable fractures of the right tibia

Internal injuries were severe The lungs of all 4 guineapigs projected into water at velocities of 104 ft per sec or more were extensively damaged, much as in cases of severe blast injury Subpleural hæmorrhages were found on all surfaces of both lungs, in many areas they were confluent and in places (particularly on the posterior surfaces) they formed a distinct pattern of " rib markings " There were patches of subpleural emphysema and occasional small tears on the costal and diaphragmatic surfaces Microscopically there was generalised pulmonary disruption with massive hæmorrhage (fig 7), the traumatic emphysema amounted in places to cavitation Intervening small areas of collapsed or of relatively normal lung tissue were present Many bronchi were partially or completely occluded by plugs consisting of material staining with periodic acid Schiff reagent and sh[illegible]f bronchial epithelium which seemed to have [illegible]ped from the bronchial wall with disruption of [illegible]vidual cells, occasionally it appeared as if the [illegible]onchial epithelium had moved distally, blocking alveolar ducts and even alveoli (fig 8) Some large pulmonary blood vessels and lymphatics were torn across, whereas others were abnormally congested In all the guineapigs the upper lobes tended to be less severely affected than the middle and lower lobes

Similar but localised pulmonary lesions were found in guineapigs projected into the water at velocities of 75–101 ft per sec Two guineapigs projected at 66 and 73 ft per sec showed only patchy subpleural ecchymoses and congestion of the pulmonary vessels The control guineapig projected into cotton-wool developed a single subpleural ecchymosis on the anterior margin of the left upper lobe The lungs were also congested but otherwise intact, and the only other lesion found was a small hæmorrhage into the perinephric fat

Throughout these experiments no difference in lung pathology could be seen between the anæsthetised and dead guineapigs, in none of the former was there any evidence of death by drowning

Necropsy findings other than in the lungs can be summarised briefly Most of the guineapigs had a few small hæmorrhages into the muscles of the chest wall Hæmothorax was present in 6 cases, hæmopericardium in 3 Cardiac distension, particularly of the right ventricle was obvious in 4 guineapigs, and in 2 there was a small tear in the wall of the right atrium close to the point of entry of the inferior vena cava In the abdomen there was free blood in the peritoneal cavity in 10 guineapigs, ruptures of the stomach or intestinal tract in 7, lacerations of the liver in 7, a splenic tear in 1, and multiple mesenteric or retroperitoneal hæmorrhages in 7 The diaphragm remained intact Skeletal injuries seen in the radiograph were not extensive, they were a constant finding only in guineapigs projected into water at the highest velocities Minor fractures of the skull were found only twice, spinal fracture dislocations appeared in 3 cases, costovertebral dislocations in 2, and various limb fractures in 5

Owing to technical difficulties a continuous electrocardiographic record was obtained in only 1 guineapig abnormal cardiac activity being recorded after impact with the water at a velocity of 95 ft per sec There was complete atrioventricular dissociation, but ventricular activity persisted for some minutes in an altered but regular form, evidently controlled from a ventricular ectopic focus

Conclusions

(1) The experiments suggest that severe internal injuries may be expected as a result of impact with a

water surface The pulmonary and intra abdominal lesions are essentially the same as those found in the Comet victims The latter did not have "rib markings" but this is probably acceptable as a species difference Such markings are readily produced in guineapigs not only by blast and impact but also by explosive decompression and even coal gas poisoning whereas in man many cases of severe lung damage from air blast and from body impact have not shown this phenomenon Nor is it a feature of coal gas poisoning in man

(2) The degree of lung injury from water impact is related to the incident velocity the critical velocity for generalised injury in the guineapig being about 104 ft per sec This is close to the predicted value but owing to the approximate nature of the calculations this must be regarded as largely fortuitous

(3) Living anæsthetised guineapigs may be killed by the impact and show no evidence of death by drowning

Skin Lesions

ELBA ACCIDENT

In 14 of the 15 bodies recovered from the sea at Elba there was a similar type of skin damage The affected areas had the following features

(1) They were red and their peripheral margins were distinct but irregular in outline

(2) In some bodies they were traversed by parallel-sided bands of apparently undamaged skin

(3) In most cases the affected parts were beneath the clothing found on the cadaver when removed from the sea.

(4) There was no evidence of scorching or singeing of hair or epidermis but in places there was some exfoliation.

(5) None of the clothing was burnt or decomposed in any way

(6) Some of the areas of skin damage corresponded closely to yellowish stains on the adjacent and overlying garments.

13 bodies showed this type of injury on the back and/or buttocks 3 of these bore further lesions: one on the calf a second on the thigh and temple and the third on a small area under the chin Of the remaining 2 bodies 1 that of a corpulent adult male had a large area of altered skin on the front of the trunk only and the last body was completely unmarked in this respect

Histologically these lesions showed no signs of vital reaction The epidermis was in some areas intact in others separating or absent Epidermal cells usually showed a vacuolar change An accumulation of brown pigment like granular material in the basal cells and occasionally in malpighian and horny layers was noted in 4 of the 5 specimens from pale-skinned European bodies The dermis showed well preserved glandular and hair follicle elements but severe degenerative often coagulative change in the collagen (Fornari 1954)

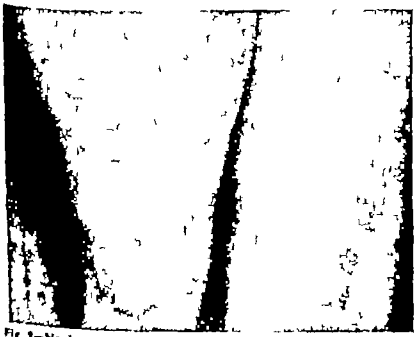

Fig 9—Naples accident: body C. Pattern of skin darkening on front of thighs with "shadowing" of garments.

NAPLES ACCIDENT

3 of the bodies recovered had obvious skin changes quite different from those described in the victims of the previous crash. In each case the lesions appeared as a brown or smoky coloration in exposed parts of the body with sharply defined margins corresponding to the edges of garments In 1 body the darkened areas were the back and front of the trunk and thighs, with an encircling pale band corresponding to the level of the waistband of the skirt the darkening was sharply limited above at a level corresponding to the lower edge of a brassiere while the lower edge was not well defined In a second case (adult male) the back showed a clear T-shaped pale band underlying the waist and perineal straps of a patent suspensory garment The third body showed very clearly intense darkening of the areas between stocking tops and corset, with pale bands corresponding to the outlines of the suspenders (fig 9) There was in this case less intense darkening of areas underlying the main parts of the stockings, and sparing of the skin under the reinforced band at the upper end This "shadowing" of garments was less marked on the back than the front of the thighs The 2 remaining bodies showed a slight darkening of the skin of the legs, not clearly delineated above but cut off sharply at the level of the shoes in one case, and the level of short socks in the other The clothes bore no signs of fire or chemical staining The affected areas of the skin were not those one would normally expect to find "tanned" by sun bathing during life

Histologically the skin was normal In view of the long interval between death and necropsy the preservation was remarkably good Pigment granules were visible in the normal situation in skin from both pale and dark areas of the bodies, with no visible difference in quality *quantity, or distribution*

CAUSATION

The first consideration appears to be whether the two types of lesions (called for convenience "burns" and "darkening" in the Elba and Naples accidents respectively) can be attributed to the same cause or causes In studying this matter the following conclusions were reached:

(1) Neither type of lesion appeared to be familiar to forensic pathologists, and no immediate cause could be assigned to either when first seen.

(2) In both accidents most of the bodies were affected but the types of skin change were quite distinct—i.e., "burns" only in Elba bodies "darkening" only in the Naples bodies

(3) There was a fundamental difference in distribution of lesions "burns" affecting predominantly clothed areas, and "darkening" involving exposed skin only

(4) There was histological evidence of tissue destruction in the "burns" only

(5) In neither case was there any evidence of exposure to flame or searing temperatures.

In view of these facts it was felt that separate causes are possible and indeed probable for the different types of lesion Was there any factor present in one accident and absent in the other which might give a clue to the ætiology of the injuries? The only obvious difference was that the length of time that the bodies were in the sea differed greatly four hours at Elba and twenty two hours at Naples

Ætiology of "Burns"

In the course of discussions with Dr Teare the following possible causes were considered

(1) *Contact with hot metallic surfaces not hot enough or acting long enough to cause singeing*—This is improbable because it would imply that all but 2 of the bodies lay oriented back

down to the surface, which was uniformly heated to a sub singeing temperature, or that contact was limited to a short time in all the cases It also seems unlikely that in only 1 instance was an unclothed area burnt in spite of such parts being exposed more directly to any heat source

(2) *Contact with hot liquid or vapour in the aircraft*—The location of the lesions would again imply similar orientation of 13 of the 15 victims Of the possible liquids, engine oil, tea, and coffee have been excluded by chemical examination of the clothing Hydraulic fluid, though not definitely ruled out, is a most unlikely agent when its volume, temperature, area of spread, and access to the passenger cabin are considered. Once more the sparing of exposed parts is unexplained by this theory

(3) *Abrasion on impact*—This is considered to be ruled out on the basis of absence in the Naples victims, the distribution of the lesions, and the macroscopical and microscopical appearances

(4) *Exposure to high intensity flash from an aircraft fire during free fall of the bodies*—This is unlikely, and is incompatible with the location of injury in covered areas

(5) *Fall through flame from burning fuel in or near the aircraft*—This cannot be reconciled with the absence of scorching or charring of clothes and skin

(6) *Chemical burning*—Battery fluid can be excluded on the grounds of lack of access and failure of chemical tests on clothing Two highly suspect substances known to be present are kerosene fuel (paraffin) and methyl bromide (used in fire extinguishers in engine and equipment bays of the aircraft) The former was present in large quantities and is known to be a skin irritant under some circumstances, moreover, the clothing on the bodies smelt strongly of kerosene However, exposure of skin to kerosene and sea water soaked clothing produces no lesions, at least during the relevant period Methyl bromide can certainly burn living skin (von Oettingen 1946), and, being highly volatile, is difficult to detect in clothing However, in experiments made at the R.A.F Institute of Pathology and Tropical Medicine only 1 of several freshly killed guineapigs showed any reaction to being clothed over the shaved abdomen, sprayed with kerosene and methyl bromide, and then floated in sea water The solitary finding was slight congestion of the dermal capillaries, with occasional extravasated red cells—quite unlike the human material from Elba

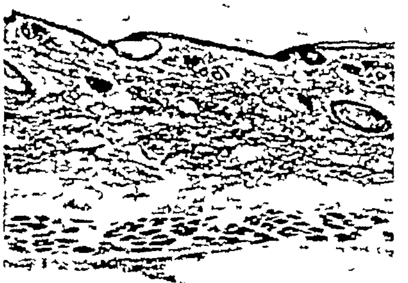
Fig 10—Guineapig skin normal appearance. (Hæmatoxylin and eosin ×28)

(7) *Contact with a surface layer of sea water heated by burning kerosene*—Experiments suggest that this is the most probable explanation of these " burns " A film of kerosene burning on the surface of a large expanse of water produces temperatures of 100°C at surface level, 70–100°C at a depth of $^1/_4$ inch, 30–50°C at a depth of $^1/_2$ inch, and no change (18°C) at or below 1 inch from the surface (Royal Aircraft Establishment 1954) In experiments at Farnborough, recently killed guinea pigs were " clothed " with bands of various types of material over depilated abdominal areas and allowed to float on the surface of a water tank 35 ft in diameter Kerosene was poured on to the surface and ignited In spite of all the bodies having been enveloped in an unapproachable conflagration (air temperatures of 500°C $^1/_2$ inch above the water surface) the only sign of their having been exposed to fire was scorching of the distal parts of the limbs and ears in 3 of 6 animals It was apparent that these relatively rigid members projected above the water in a way unlikely to be paralleled by any portion of the human anatomy None of the clothing was burned Underneath the fabric, which was in most cases stained in a similar way to the garments seen at Elba, pinkish areas of indurated skin could be seen and palpated These ar [illegible] e or both flanks, corresponded to the uppermost [illegible] the floating guineapig in each case Comparison [illegible] l preparations of the skin from affected and [illegible] showed relatively little change of the epidermis but very pronounced swelling and coagulative necrosis of the dermal collagen (figs 10 and 11) Glandular structures and hair follicles were still recognisable

It appears that clothed bodies, floating in water where a kerosene film is burning, may be scalded by the heated surface layer of water about $^1/_2$ inch in depth, without singeing or charring of the clothing or hair, provided that the garments are wet and that no part projects above the surface

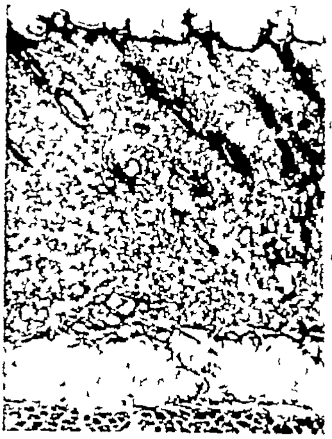
Fig 11—Skin from flank of dead guineapig floated in water covered by burning kerosene, showing dermal thickening and coagulative necrosis (Hæmatoxylin and eosin ×28)

Little is known of the orientation of a floating freshly dead cadaver killed by means other than drowning It is most probable that the position is face down, with the limbs and head dependent It was recorded by those who recovered the bodies at Elba and Naples that in each case all but one of the bodies was floating back uppermost In such circumstances the scalded areas in a person floating in a kerosene fire would correspond closely to those areas of the back predominantly affected in the Elba victims The unidentified yellow stains on the clothing are, of course, also accounted for by this theory, but their exact nature remains obscure.

Ætiology of " Darkening "

This type of skin marking could be ascribed to one or more of three fundamental types of change application of an exogenous coloured material, formation of an intradermal or intra epidermal coloured substance from degradation of structural elements, or intensification of the normal pigment of the skin

An exogenous coloured material was excluded by the failure of various solvents to remove the colouring, and the absence, in unstained frozen sections, of any apparent surface deposit of coloured matter In stained and unstained sections there was no evidence of structural or colour abnormalities other than slight post mortem change which was the same in dark and pale areas Darkening of pre existing melanin in human skin under certain conditions, which could occur in life or after death, was described by Meirowsky (1909) This and subsequent work (Lignac 1923, Miescher and Minder 1939, Blum 1948) has shown that pigment can be darkened in dead skin by exposure to sunlight or to long wave ultraviolet rays over the 3000–4200 Å range, and by maintaining pieces of dead skin at a temperature of 56°C for one to three days

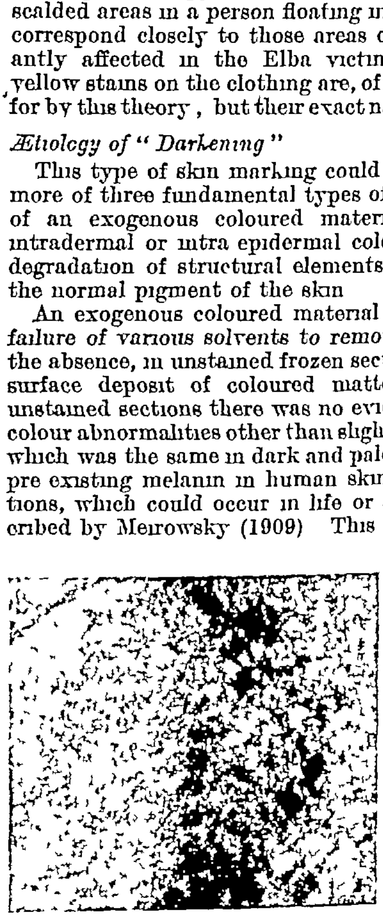
Fig 12—Pigment darkened in recently dead skin of human thigh after six hours' exposure to emission of carbon-arc. Left half of specimen was shielded from light. (×2 approx)

In experiments made at the National Physical

Laboratory with the kind coöperation of Mr J S Preston and others in the Radiant Energy Section pieces of human skin which had been dead for about twelve hours were exposed to a light source (a cored carbon arc) with an emission similar in long wave ultraviolet content and intensity to summer sunshine Part of each piece of skin was shielded with aluminium foil Well defined darkening of the pigment was produced after two and a half hours exposure and was little changed by prolongation to six hours (fig 12)

It is difficult to imagine circumstances in the accident which would give rise to a short-duration 'flash emission of sufficient energy to cause the skin changes seen in the Naples bodies It is known that they floated in the sea for about twenty two hours, including the greater part of a clear sunny day, and in all probability the skin markings were due to post mortem darkening of pigment in unclothed areas as a result of ultraviolet irradiation The sites of maximal intensity of pigmentation were as might be expected from the attitude of the bodies when found

Conclusions

Reconstruction of the events from medical evidence alone must of necessity, be largely a question of relative probabilities but the condition of the bodies recovered from the sea can be explained most satisfactorily on the basis that the injuries were inflicted in three distinct phases in the aircraft, on impact with the sea, and while the bodies were floating in the water

Head injuries including multiple fractures of the vault and base of the skull were an outstanding feature Extravasations of blood showed that most of these occurred in life The observations of Merkel (1920) and Lemke (1928) on deaths from jumping into water show that head injuries of this type do not occur regularly in such cases and our experimental findings are in full agreement with this. We conclude that the head injuries together with certain abrasions and at least some fractures of the thoracic cage were acquired in the aircraft apparently as the result of an extremely violent upward and forward displacement of the seated occupants at the moment of the initial failure Safety belts would not have been fastened half an hour after take off, and these injuries could be expected to result from violent impact with the inside of the aircraft and its furnishings They were alone sufficient to cause death and were presumably the source of fat embolism in those cases in which it was found This violent movement may have contributed to the internal injuries but is not thought to have been the major cause

Initially there was much speculation about the origin of the displacement forces Calculations by aerodynamicists showed sudden deviation from the line of flight due to malfunction or misuse of controls unlikely to be sufficiently violent to cause such numerous skull fractures The latent energy in a pressurised cabin of large volume has been calculated as being equivalent to that contained in about 100 lb of high explosive (Walker 1950) and the hazard to occupants *of displacement by the rush of* escaping air during sudden depressurisation has long been appreciated (Sweeney 1944 Fulton 1948) The dramatic effects of such failure have been illustrated by model cabin tests with anthropomorphic dummies at the Royal Aircraft Establishment We conclude that the most probable cause of the upward and forward motion imparted to the occupants of the aircraft was a sudden cabin failure In fact reconstruction of the Elba wreckage demonstrated beyond doubt that an initial structural failure of this kind did take place and extensive examination and testing of Comet aircraft have supported the belief already expressed that the Naples accident followed a similar pattern There is no definite evidence to show whether or not the lungs were damaged by the explosive decompression but for reasons already given this is considered to be unlikely

As the aircraft broke apart all or most of the passengers were ejected, presumably at different altitudes and fell into the sea All the available evidence indicates that forces generated by impact with a water surface after such a fall must cause grave injury to internal organs The nature of the internal injuries in the bodies recovered including the pulmonary lesions is consistent with their having been caused for the most part in this way In the circumstances any pre-existing visceral damage due to explosive decompression or to impact within the aircraft could not be identified Other injuries probably received at the same time include fractures of the limb bones and spine and further damage to the thoracic cage Experimental dropping of full scale clothed dummies has confirmed that impact with the sea rather than free fall through the air was also responsible for the extensive loss of clothing (Royal Aircraft Establishment 1954) It is just conceivable that a few passengers remained within a segment of the fuselage until it hit the sea This is unlikely to have afforded much protection but might possibly explain why some of the bodies, all from rearmost seats had retained most of their clothing

Finally, while floating on the sea 14 of the Elba bodies were subjected to post mortem scalding of the skin It is improbable that they fell into an existing kerosene fire, because there was no singeing or burning of their clothing or hair ; more likely the fire started after they had fallen into an area covered by a kerosene film The bodies from Naples showed no scalds but instead a pattern of post mortem darkening of the pigment (the Meirowsky phenomenon) as the result of exposure to the bright sunshine of April 9

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REFERENCES

Armstrong H G (1936) *J Aviat. Med* 7 2
Baker J R (1946) *Quart J micr Sci* 87 441
Benson O O (1953) Aeromedical Panel Advisory Group for Aeronautical Research and Development N.A.T O Third General Assembly, London (Unpublished)
Benzinger T. (1950) German Aviation Medicine in World War II Prepared by the Department of the Air Force Washington p 404
Bergeret, I , Giordan P, (1939) *C.R. Soc Biol Paris* 131 1041
Blum, H F (1948) *In* The Biology of Melanomas. Edited by M Gordon New York
Cameron G R, Short R H D., Wakeley C. P G (1942) *Brit J Surg* 30 49
Clemedson C. J Granström, S A (1950) *Acta physiol scand.* 21 131
Cole C R Chamberlain, D M, Burch B H, Kemph, J P, Hitchcock, F A. (1953) *J appl Physiol* 6 96
Edelmann A., Whitehorn W V Lein, A Hitchcock, F A (1946) *J Aviat Med* 17 596
Eggleton P Elsden S R, Fegler J Hebb C. O (1945) *J Physiol* 104 129
Flying Personnel Research Committee (1942) Report no 43
Fornari A (1954) Evidence given at the Comet Aircraft Accident Inquiry London
Fryer D I (1953) Aeromedical Panel Advisory Group For Aeronautical Research and Development, N.A.T O Third General Assembly London (Unpublished)
Fulton J F (1948) Aviation Medicine in its Preventive Aspects London p 93
Garsaux P Richou M. Laurent J (1939) *Bull Acad Med Paris*, 122, 101
Gosselin L (1847) *Mém. Soc Chir Paris* 1 201
Greaves, F C., Draeger R, H Brines O A. Shaver J S Corey E. L. (1943) *Nav med Bull Wash* 41 339
Hadfield G Ross, J M. Swain R H A Drury White J M (1940) *Lancet* ii, 478
Hess G M, (1944) *J Aviat Med* 15 77
Heim, J W (1938) *J aero. Sci* 5, 180
Hitchcock F A (1953) United States Air Force W.A.D.C. Tech Report 53 191
Hooker D R. (1924) *Amer J Physiol* 67 219
Lignac G O E. (1923) *Virchows Arch.* 240 383
Lovelace W, R Gagge, A P (1946) *J aero. Sci* 13 143
Meirowsky E (1909) *Frankfurt. Z Path.* 2 438

References continued overleaf

COMPLICATIONS OF CHLORPROMAZINE THERAPY IN 800 MENTAL-HOSPITAL PATIENTS

J LOMAS
B.A , M B Camb , D P M
ASSISTANT PSYCHIATRIST

R H BOARDMAN
M A , M.B Camb , D P M
SENIOR REGISTRAR

MORRIS MARKOWE
M D Lond , D P H , D P.M
CONSULTANT PSYCHIATRIST

SPRINGFIELD HOSPITAL, LONDON

CHLORPROMAZINE has been increasingly used in both psychiatry and anæsthetics since 1951 The early investigations of Courvoisier et al (1953) into its pharmacological effects on animals suggested that it was relatively non-toxic, but subsequent trials on man have not confirmed this, and Burn (1954) suggests that it is toxic to animals Complications have been reported which, though not perhaps justifying all the precautions advocated by the earlier workers suggest that great care should be taken in administering chlorpromazine

The complications can be divided into side effects and toxic reactions The side effects are usually due to the pharmacological action of chlorpromazine on the autonomic nervous system and are therefore necessary concomitants of the treatment, whereas the toxic reactions are observed in relatively few patients and are due to idiosyncrasy The distinction is not absolute, there being some overlap between the two types of complication

Side-effects Previously Reported

Cardiovascular system —The most important side effects concern the cardiovascular system Tachycardia and pallor are almost unavoidable, at least in the early stages of treatment, and are sometimes associated with a fall in blood pressure which may give rise to vertigo, weakness, and syncope For this reason the earlier workers advocated rest in bed in the initial stages of treatment (Delay and Deniker 1952, Sigwald and Bouttier 1953a, Anton Stephens 1954), but this is now considered unnecessary (Garmany et al 1954, Lomas 1955)

Gastro intestinal tract —Gastro intestinal disturbances are common, dryness of the mouth is mentioned in almost all reports, and constipation, diarrhœa, nausea, and vomiting are common Nausea and vomiting are perhaps surprising in view of the proved anti emetic action of chlorpromazine (Friend and Cummins 1953, Moyer et al 1954a) Lehmann and Hanrahan (1954) report an increase in appetite and a gain in weight, these changes Elkes and Elkes (1954) correlate with clinical improvement

Respiration —Courvoisier et al (1953) found that small doses stimulated, and larger doses depressed respiration in rabbits This difference of action in different dosages may explain the conflicting reports on the effects of chlorpromazine on respiration in man Lehmann and Hanrahan (1954) found no change, Staehelin and Kielholz (1953) depression, and Bensoussan and Klein (1953) severe dyspnœa

Micturition —Lehmann and Hanrahan (1954) found an increased frequency of *micturition* but no other abnormality This is confirmed by Moyer et al (1954b)

Central nervous system —A parkinsonian like syndrome is reported by Lehmann and Hanrahan (1954), Azima and Ogle (1954), and Anton Stephens (1954), who, probably correctly, attribute it to overdosage Anton Stephens (1954) and Winkelman (1954) report an increased tendency to dream.

Local irritation —Intramuscular chlorpromazine produces local irritation *at the site of the injection*, this may cause considerable discomfort (Anton Stephens 1954, Winkelman 1954 Charatan 1954), which can be minimised by dilut *the injection* (Deschamps 1952, Staehelin and Kielholz 195 Arnold et al. 1953)

There is no change in the blood sugar level (Staehelin and Kielholz 1953, Lancaster and Jones 1954), electrocardiogra (Friend and Cummins 1953 Moyer et al 1954b), or elect encephalogram (Terzian 1952, Flügel 1953)

Toxic Reactions Previously Reported

Acute toxic reactions have been singularly rare, but Deni (cited by Winkelman 1954) had a patient who attemp suicide by taking 750 mg of chlorpromazine and lapsed into coma but recovered uneventfully within a few days. Charatan (1954) and Lomas (1955) recorded 1 and 9 deaths respectively in their series, but in none of these cases could chlorpromazine be implicated with any conviction In 2 patients, however, both of whom had liver disease, chlorpromazine was considered to be at least a contributory cause of death (Boardman 19 Deschamps 1952)

Hepatitis

The most serious complication is toxic hepatitis Garm et al (1954) reported abnormal liver function tests, and b salts in the urine, but no manifest jaundice in 3 of 29 ca Charatan (1954) had 1 case in 42, and Winkelman (1954) in 142 (in 1 of these liver biopsy showed chronic liver dama Lehmann and Hanrahan (1954) treated frank jaundice in of their 71 cases but reported slightly abnormal liver funct tests in 50%

On the other hand, Elkes and Elkes (1954) had 1 case jaundice in 27 but found no abnormality in liver funct tests done at fortnightly intervals in the 26 other cases, Moyer et al (1954b) found hepatic function normal in cases Azima and Ogle (1954) report 8 cases in 100, but th was an outbreak of mild infective hepatitis at the tim Eagles (1955) reports 3 cases in 18—the highest incidence recorded Both Garmany *et al* (1954) and Elkes and E (1954) continued treatment with chlorpromazine after interval and observed no untoward effects

Blood Picture

Rizzo and Russo (1953), in carefully conducted inve gations on 15 patients, found after a single injection chlorpromazine an almost constant slight decrease in number of red cells and in the amount of hæmoglobin, leucopenia, lymphocytosis, neutropenia, and eosinop This change was observed three hours after the injection. the blood tended to return to normal in twelve ho Similarly the erythrocyte sedimentation rate (E.S.R.) three hours after the injection and tended to return to nor in twelve hours This difference in the findings after three after twelve hours may possibly explain the different res of other workers

Friend and Cummins (1953), Lehmann and Hanra (1954), and Charatan (1954) found no change in the bl picture Elkes and Elkes (1954), who did full blood-co fortnightly, found polychromatic cells with basophil stippling in 1 case and neutropenia in 1 other Staehelin and Kielholz (1953) and Delay et al (1952) agreed with Rizzo and Ru (1953) in finding an initial neutropenia returning rapidly normal, but found no abnormality in the red-cell co Anton Stephens (1954), on the other hand, found a leucop in half his cases and a raised E S.R in almost all Lo (1954) reports 1 case of agranulocytosis, and F J A (personal communication) mentions 8 others in the Unit States Of these, only 1 has so far been published (Bo 1955), of the unpublished cases 1 proved fatal but all the others were cured with corticotrophin

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FLIGHT-LIEUT ARMSTRONG AND OTHERS

REFERENCES—*continued*

Merkel, H (1926) *Dtsch Z ges gerichtl Med* 8 517
Miescher, G , Minder H (1939) *Strahlentherapie*, 66 6
Moritz, A R (1954) The Pathology of Trauma 2nd ed , London , p 207
O Reilly, J N , Gloyne S R (1941) *Lancet*, ii, 423
Osborn G R (1941) *Brit med J* i 506
Pearse, A G E (1954) Histochemistry, Theoretical and Applied London , p 445
Penney, W G , Bickley, W G (1943) Min of Home Security Report R C 376 (Unpublished)
Polak, I B., Adams B H (1932) *Nav med Bull , Wash* 30, 165
Richardson E G (1948) *Proc phys Soc Lond* 61 352
Robb Smith, A H T (1941) *Lancet*, i, 135
Rotondo G (1953) *Riv Med aero* 16 153
Royal Aircraft Establishment (1954) Comet Accident Report Accident Note no 269
Rushmer R. F Green, E L Kingsley H D (1946) *J Aviat Med* 17 511
— Hass, G M (1946) United States Army Air Force School of Aviation Medicine Research Project 471 Report no 1
Stewart W K , Spells K E Armstrong J A (1955) *Nature Lond* 175 504
Sweeney, H M (1944) *Air Surg Bull* no 10 1, 1
Vavala D A (1954) United States Air Force, School of Aviation Medicine, Unnumbered Report
Violette F (1954) *Med Aero* 9, 223
ingen W F (1946) *Nat Inst Hlth Bull* no 185, p 23
P B (1950) *J R aero Soc* 54 235
E R P (1942) *Brit J Surg* 30, 38
J V Tunbridge, R E (1943) *Lancet* i 297
E (1928) *Dtsch Z ges gerichtl Med* 12 346
S (1940) *Lancet* ii 219
(1941) *Proc R Soc Med* 34, 171

Pyrexia in the first few days treatment has been noticed y most workers (Staehelin and Kielholz 1953 Garmany et al. 1954 Lehmann and Hanrahan 1954) Sigwald and Bouttier 1954b) and Charatan (1954) attribute it to local inflammation it the site of injection.

Skin eruptions either urticarial or maculopapular are eported by Broussolle and Hamoneau (1953) Azima and gle (1954) Winkelman (1954) and Lehmann and Hanrahan 1954), the last-named in 13% of their cases.

Epileptic fits —Anton-Stephens (1954) mentions that 1 st leucotomy patient had epileptic fits but attaches no gnificance to this finding Lehmann and Hanrahan (1954) te that 1 patient who had been given 2 ml. of nikethamide fter chlorpromazine developed status epilepticus

Present Survey

Our report is based on 800 patients (260 male and 40 female) treated with chlorpromazine in Springfield Hospital between November 1953 and the end of 1954 e patients were not questioned about any untoward fects hence any complications noted were either a ult of spontaneous complaint by the patients or *served by the nurses and doctors.*

Toxic effects were all recorded on a pro forma with a te of the dosage, total amount of chlorpromazine ministered at the time of the reaction duration of atment and any possible alternative ætiology to lorpromazine.

Though all types of mental cases were treated the at majority were *acute or chronic psychoses* The age varied considerably from patient to patient but e most commonly adopted plan was to start with 150 daily and to increase rapidly to 300 mg daily The seriously disturbed patients received smaller doses, d a few patients had their dosage increased to 800 mg ily The duration of treatment varied from a few eks to several months The great majority of patients eived the chlorpromazine by mouth and were treated bulant from the start A minority underwent electro vulsion therapy concurrently and most patients were eiving barbiturate sedation No other form of rapy could account for the toxic reactions

SIDE EFFECTS

rdiovascular System

The tachycardia noted by most previous workers was esent also in this series and when looked for specifi lly was found in almost all patients in the initial ages of treatment. Only extremely rarely was it ociated with palpitations or did it give rise to any ontaneous complaint from the patient Pallor was s common.

Minor hypotensive symptoms were complained of by me patients in the early stages of treatment but ncopal attacks were extremely rare With 1 exception e few which did occur were all in elderly or arterio rotic patients For this reason it was considered necessary to treat patients in bed unless their mental ndition necessitated it with the *exception of the* derly and the arteriosclerotic

Gastro intestinal tract —Of gastro intestinal complaints ness of the mouth and constipation were far the most mmon Nausea vomiting, and diarrhœa occurred too rely for chlorpromazine to be implicated A pro unced increase in appetite and weight were noted, rticularly in patients given chlorpromazine for a long me One patient who had not previously shown onounced fluctuations in weight gained 5 st in as any months

espiration —No respiratory anomalies were noted

Micturition —Frequency of micturition was observed. casional incontinence of urine and more rarely still of ces occurred Incontinence seems to be due to over sage because it rapidly disappears if the dosage is educed

Central nervous system —The parkinsonian like syn drome was also occasionally noted and similarly responded to a reduction in dosage

Local irritation at the site of injection occurred but was not of great importance in this series because the great majority of patients received the chlorpromazine by mouth

Both subjective complaints and observed disturbances were much less common in disturbed psychotic patients than in others and the more chronic the psychosis the less was the incidence of side effects. The only exception to this was the gain in weight, which took place in all types of patient if they were treated with chlorpromazine for a long time The predominance of psychotic patients in this series may explain the altered emphasis on the various side-effects from that of other investigators

TOXIC REACTIONS

The total number of toxic reactions recorded in the 800 patients was 59 (7.4%) Of these 48 (8.9%) occurred among the women and only 11 (4.2%) among the men. This difference varies in the different toxic reactions (see below)

Jaundice

All patients in whom jaundice arose during chlor promazine therapy are included no cases arose after completion of therapy Unfortunately the study is clouded by the coincidental appearance of infective hepatitis in patients not receiving chlorpromazine The two conditions were clinically and biochemically indistin guishable but the incidence was significantly higher in the chlorpromazine population only 3 cases occurring in the rest of the hospital population of over 2000 patients

There were 11 cases of chlorpromazine jaundice (1·4%), 4 male (1.5%) and 7 female (1.3%) No age group was immune At the onset chlorpromazine had been administered for from sixteen to thirty three days (mean twenty two) The daily dosage at that time and the total quantity administered varied widely and were not significant All the patients received the chlor promazine by mouth but 5 had started with intra muscular injections for a few days The appearance of jaundice was regarded as an absolute contra indication to the further use of chlorpromazine The jaundice lasted from one to twenty six weeks but if the 2 most severe cases (in which the jaundice lasted thirteen and twenty six weeks) are excluded the mean duration was two weeks

In 7 instances icterus was the presenting symptom associated in 1 case with pyrexia and gastro intestinal disturbance and preceded by four days in 1 other case by ephemeral asymptomatic pyrexia It is possible that ephemeral pyrexia had been missed in other cases Prodromal fever and malaise lasting one or two days ushered in 3 further cases 1 of which had already shown a morbilliform rash for a week The remaining case showed gastro intestinal symptoms gradually remitting nine days before jaundice on the twenty second day 6 of the patients presenting with icterus felt relatively well at onset including the 1 fatal case Anorexia was severe in 2 other cases

During the jaundice itching was common the liver was somewhat enlarged and slightly tender; the stools varied in colour from normal to off white; and the urine contained bile salts and pigments

The 3 mildest cases were not studied biochemically In the 8 others thymol turbidity colloidal gold and Takata Ara reactions and plasma protein estimations showed no abnormality The plasma alkaline phospha tase and serum bilirubin levels and the bromsulphalein clearance (when tested) showed consistent changes which reflected the *clinical state* The alkaline phosphatase showed peak values of 15-70 King Armstrong units per 100 ml (normal 2-12) and the serum bilirubin 3 23 mg per 100 ml (normal 0 5) The "direct" component of the serum-bilirubin was invariably 2–2½ times as great as the "indirect"

9 cases ran an uneventful course to recovery Of the 2 other patients 1, a chronic encephalitic, recovered after a stormy twenty six weeks but five months after clinical recovery still has an alkaline phosphatase level of 45 King-Armstrong units and bromsulphalein clearance of 83% only (normal 95%), the other patient, who had chronic rheumatic heart-disease, died after thirteen weeks' remittent illness (Boardman 1954)

Clinically and biochemically the jaundice is of obstructive type, but the liver in the fatal case showed central necrosis and biliary stasis, severe lobular atrophy, relative preservation of portal areas, and absence of exudate, which were interpreted as "subacute toxic hepatitis of blood borne type" The ante-mortem passive congestion of the liver did, of course, contribute to a significant degree to the central necrosis

Blood Picture

Routine blood counts were done weekly on 25 patients throughout the course of chlorpromazine No consistent general depression or stimulation of hæmopoietic tissue was found The case of agranulocytosis has already been described (Lomas 1954), where the white cell count decreased to 400 per c mm but rapidly increased to 5300 per c mm in ten days after the chlorpromazine was withheld In 4 cases there was a moderate leucocytosis increasing to a maximum in the third or fourth week of treatment, followed by a gradual decrease One case with a leucopenia of 2000 white cells per c mm was noted in the fourth week, but this soon cleared when chlorpromazine was withheld In another case a leucopenia of 3000 white cells per c mm was noted in the fifth week, but subsequent counts were within normal limits This patient had been diagnosed two years previously as having aplastic anæmia but had recovered, and the leucopenia may have been due to abnormally sensitive bone-marrow A microcytic hypochromic anæmia had been noted, with a decrease in the number of red cells from 4,680,000 to 3,000,000 per c mm by the fifth week

In more than half the cases the E S R rose to a maximum by the fourth week and then fell gradually, with a secondary rise in the seventh or eighth week in a minority There was no appreciable change in the remainder

Blood studies in 6 of the skin reactions showed definite eosinophilia (13% and 7%) in 2 These cases also showed mild leucocytosis of 11,450 and 13,600 per c mm, the eosinophil-counts being 1488 and 952 per c mm respectively Such responses, in conjunction with the clinical pictures, suggest either a hypersensitivity reaction or depression of the adrenocortical hormones

Studies of the pyrexial cases showed moderate neutrophil leucocytosis in 2 patients

Skin Reactions and Œdema

These two reactions are discussed together because they so often occurred in association 22 cases (2 8%) were noted, 19 (3 5%) among the women and only 3 (1 2%) in the men 10 cases showed skin reaction and œdema mainly of the face but sometimes of the extremities as well 8 showed skin reactions only, and 4 œdema alone 3 cases had a slightly raised temperature, but the rest were apyrexial

The skin reactions were of two distinct types The first was an erythema confined to the exposed parts of the body and noted in 8 cases It occurred at any stage in treatment and on various dosages, but 6 of the 8 cases developed in August and the 2 others in April and June This reaction was regarded as due to photosensitivity, but similar reactions among the rest of the hospital
ts, owing to the deficiency of sunlight last summer,
emely rare
second reaction, observed in 14 patients, was a
orm eruption over the entire body It came on between the fourteenth and thirty-fifth days of treatme except in 2 cases, and most of the cases arose about t beginning of the fourth week Most of the patien were receiving 300 mg daily at the time, which wou be the expected daily dosage at this stage of treatmen The total dosage received varied considerably

The rash cleared up uneventfully in about a wee whether treatment with chlorpromazine was maintain or not, and did not recur when treatment was resume Generally, when there was no œdema, treatment w continued, but, if there was any œdema, treatment wa stopped temporarily

Pyrexia

Pyrexia was observed in 16 patients (2%), all of the female, in whom the incidence was 3% The pyrexia w generally low-grade (99–100°F) but occasionally rose 105°F, and usually lasted from twenty four to forty-eig hours, whether or not treatment with chlorpromazi was continued, but rarely lasted a week There was relationship either to the dosage at the time of occurren to the total dosage, or to the mode of administration, b with 1 exception it occurred between the fifth and thi teenth days of treatment, with the highest inciden about the beginning of the second week The 1 exce tion occurred on the thirty third day of treatment a was so unusual as to give rise to doubt about whethe chlorpromazine could be implicated

Pyrexia alone was rarely considered to be a contr indication to continuing treatment with chlorpromaz

Epileptic Fits

Epileptic fits occurred in 10 patients (1 3%) 4 (1 5% men and 6 (1 1%) women and had no relationship eith to dosage at the time, to total dosage, or to duration treatment

6 of the 10 patients had had leucotomy, and 4 of the had had previous fits immediately after the operation b not for many years The 2 others had not had an previous fits None of them has had a fit since treatmen with chlorpromazine was discontinued

Of the 4 other patients 1 had arteriosclerotic dementi and although he had had no fits before treatment wit chlorpromazine he continued to have them after it w discontinued, 1 was demented as a result of a severe he injury and had a succession of epileptic fits only while was on treatment, 1 was schizophrenic and had ha occasional fits in the remote past but none for severa years before treatment with chlorpromazine and no after, and 1 was a schizophrenic who had no fits eithe before or after treatment with chlorpromazine

In only 1 of the 10 patients who had epileptic had no tendency to epilepsy been observed, but in all them fits were very rare, had been absent for a long tim and, with 1 exception, have not recurred since treatm with chlorpromazine was stopped The fits were regard as a contra-indication to continuing treatment wi chlorpromazine

Discussion

Although the side effects (as distinguished from tox reactions) which may be due to chlorpromazine a numerous, the only one of any real significance is hyp tension, and, if due caution is taken in elderly patien and those with cardiovascular dysfunction, this on rarely causes any but minor symptoms It is met wi especially during the early stages of treatment wi chlorpromazine and when the dose is increased, a thus the risk is negligible

Of the toxic reactions, jaundice and the rare blo dyscrasias are the most important, because both may b fatal Death due to jaundice has so far only be reported in cases with previous liver dysfunction, the fore this risk may be avoided by regarding such cas contra indicating chlorpromazine treatment Previ bone marrow dysfunction also contra indicates chlo promazine treatment

Whereas the dosage at the time of the toxic reaction the total dosage, and the method of administration appeared to be of no significance the duration of treatment before the reaction was much more constant The greatest incidence of pyrexia was at the beginning of the second week and both jaundice and skin reactions came on about two weeks later Only in the case of epileptic fits was this time relationship not observed Toxic reactions of any sort, again with the exception of epileptic fits, were very rare *after the end of the fifth week* although a large number of cases were treated with chlorpromazine longer than this

There are two possible explanations Some people may be particularly susceptible to chlorpromazine in which case they might be expected to show early signs of toxicity but then they would also be expected to show other signs of intolerance and this was not observed The other and more probable explanation is that the toxic effects are due to sensitisation though this is curious *in view of the known antihistaminic properties of* chlorpromazine Some support is lent to this suggestion by the development of eosinophilia in a few cases Further in those cases in which treatment with chlorpromazine was continued regardless of the toxic reaction the toxic symptoms subsided spontaneously and rapidly The sensitisation hypothesis is therefore worth further investigation

The fact that the epileptic fits had no relationship either to dosage or to duration of treatment suggests that chlorpromazine has epileptogenic properties which may lead to manifest fits in susceptible people This is to be the subject of a special study

Summary and Conclusions

The complications noted in the course of treating 800 patients with chlorpromazine are classified Such complications *may be divided into side-effects and toxic* reactions.

Of the side-effects hypotension is the only one requiring special precautions and then only in the aged and those with cardiovascular dysfunction

Jaundice blood dyscrasias skin reactions and œdema pyrexia and epileptic fits all occurred as toxic manifestations. Of these jaundice and blood dyscrasias may prove fatal and are regarded as being absolute contraindications to continuing treatment with chlorpromazine Previous liver dysfunction may predispose to jaundice and therefore should also be regarded as a contraindication to such treatment

With the exception of epileptic fits the time of occurrence of all toxic manifestations had a definite relationship to the duration of treatment but not to the dosage at the time or to the total dosage of chlorpromazine

In view of this finding and the occurrence of eosinophilia in some cases the toxic reactions are probably due to sensitisation

Epileptic fits occurred mainly in post leucotomy patients and in only 1 case were no predisposing factors detected Therefore chlorpromazine may have epileptogenic properties which may cause manifest fits in susceptible people

ADDENDUM

Since this article was written J R Tasker (*Brit med* J 1955 i, 930) has reported a further fatal case of agranulocytosis due to chlorpromazine

REFERENCES

Anton-Stephens D (1954) *J ment Sci* 100, 543
Arnold, O H, Hofmann, W (1953) *Wien med Wschr* 103 563.
Azima, H, Ogle W (1954) *Canad med Ass J* 71 116
Bensoussan I A, Klein, K (1953) *Ann méd psychol* 111 520
Boardman, R H (1954) *Brit med J* ii 579
Bolman, A I (1955) *J Amer med Ass* 157 361
Broussolle, P, Hamonneau, G (1953) *Lyon méd* 88 350
Burn, J H (1954) *Proc R Soc Med* 47, 617
Charatan, F B E (1954) *J ment Sci* 100 882

References continued at foot of next column

CONDITIONING TECHNIQUES IN THE TREATMENT OF WRITER'S CRAMP

L A Liversedge
B.A B.Sc M B Manc
M.D Duke, M.R C P
LECTURER IN NEUROLOGY

J D Sylvester
M A Camb
RESEARCH ASSISTANT
DEPARTMENT OF PSYCHOLOGY

UNIVERSITY OF MANCHESTER

The *treatment of writer s cramp is recognised as* most discouraging to patient and therapeutist alike Though included nosologically with the motor neuroses writer s cramp has hitherto defied any satisfactory ætiological interpretation in terms acceptable to neurologists psychiatrists, and psychologists

Culpin (1931) and Pai (1947) thought that writer s cramp occurred *merely as one form of disablement* in patients of psychoneurotic constitution and Glover (1949) considered it to be a typical example of conversion hysteria but Critchley (1954) affirming that writer s cramp constitutes a specific impairment of motor skill, was at pains to point out that to look upon the craft palsies as problems in psychopathology has not proved satisfying even to psychiatrists

In a recent neurological and psychological re-examination of 20 cases of writer s cramp 1 typist s cramp *and 1 violinist s cramp (to be reported)* we *concluded that* although some of the patients could be regarded as having psychoneurotic tendencies many showed no evidence of psychological disorder Indeed the pattern of mental and emotional make up of these patients exhibited the widest possible variations These observations led us to the tentative conclusion that whatever the origin of writer s cramp its persistence might be explained by the establishment of a conditioned reflex The resemblance between the writing in this condition and that observed in certain types of extrapyramidal disease invites the suggestion that this conditioning takes place at subcortical levels and the partial benefit conferred by the administration of benzhexol hydrochloride (Artane) affords some support for this suggestion It seemed from the clinical evidence that although the loss of acquired motor skill represents a reaction to a total situation involving the *act of writing the sensori* motor circuit could be regarded in terms of afferent stimulus and motor effect Close observation of the development of the cramp during the act of writing revealed that it tended to arise when the pen or else the writer s hand touched the writing surface and was then intensified by the movements of the fingers and thumb as *writing proceeded The trigger stimulus for the condi*tioned reflex should then be one or both of the following (1) tactual stimulus of the pen and (2) tactual stimulus of the hand touching the writing-surface The motor

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DR LOMAS AND OTHERS: REFERENCES—*continued*

Courvoisier S Fournel J Ducrot R Kolsky M Koetschet P (1953) *Arch int Pharmacodyn* 92 305
Delay J Deniker P (1952) Comptes rendus du Congrès des médecins aliénistes et neurologistes de France et des pays de Langue française, Luxembourg July 21-27 1952 p 7
— — Harl J M (1952) *Ann méd psychol* 110 267
Deschamps A (1953) *Pr méd* 60, 944
Lasker J H (1953) *Brit med J* i 48
Elkes, J Elkes C (1954) *Ibid* ii, 560
Flügel F (1953) Deutschen Pharmakologen Kongress Bonn Oct 4-7 1953
Friend D G Cummins J F (1953) *J Amer med Ass* 153 480
Garmany G May, A R Folkson A (1954) *Brit med J* ii 439
Lancaster N P Jones D H (1954) *Ibid* ii 565
Lehmann H E Hanrahan G E (1954) *Arch Neurol Psychiat Chicago*, 71 227
Lomas J (1954) *Brit med J* ii 358
— (1955) *Ibid* i 879
Moyer J H Kent B Knight R W, Morris G Dixon M Rogers P Spurr C (1954a) *Amer J med Sci* 227 171
— — — — Huggins R Handley C A (1954b) *Ibid* 227 283
Rizzo L M, Russo S (1953) *Rass Stud psichiat* 42 632 707
Sigwald J Bouttier D (1953a) *Ann méd* 54 150
— — (1953b) *Pr méd* 61 60
Staehelin, J E, Kielholz P (1953) *Schweiz med Wschr* 83 581
Terzian (1952) *Rass Neur veg* 9 211
Winkelman N W jun (1954) *J Amer med Ass* 155 18

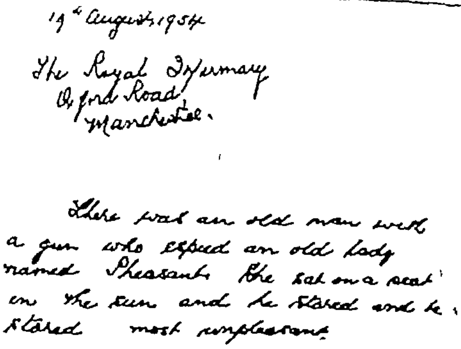
effect varies from case to case but tends to have two principal components (1) a tremor of variable rate and amplitude, and (2) a spasm of the muscles of the hand, forearm, and even the upper arm, variable in its extent and intensity but invariably accompanied by excessive pressure of the thumb upon the pen

Proceeding on the assumption that a conditioning mechanism is at work we reasoned that it might be possible to disturb the reflex by the administration of a sensory counter stimulus whenever the motor effect took place After some tentative efforts with feed-back from needle electrodes placed in the muscles of the forearm, simpler techniques were evolved to deal with the tremor and the pressure of the thumb on the pen It was felt that by attacking these primary manifestations of the motor dysfunction we might break down the whole sensorimotor chain

To date we have completed treatment of 6 patients with writer's cramp* and 1 with typist's cramp 2 other patients with writer's cramp are still under treatment It seems appropriate to give in some detail the histories and course of 2 of the patients with writer's cramp and of the 1 case of typist's cramp, The 2 writer's cramp cases were selected because 1 had a definite history of psychiatric abnormality and the other was a man whose history and personality were devoid of recognisable psychological disturbance, and in both cases the disturbance of writing comprised both tremor and spasm The case of typist's cramp is interesting in illustrating a modification of the technique to suit a particular motor problem where the principal disorder was a flexor spasm of certain fingers

Writer's Cramp

Case 1—A female typist, aged 49, an intelligent but anxious woman who in the first interviews concealed many facts of her history, passing herself off as single when in fact she had been married and divorced, and had numerous social and personal disturbances in her life The evolution of her cramp was at once interesting and complex She took to bookkeeping at the age of 18, and for the next 26 years experienced no trouble with her writing although occupied for six hours each day in ledger work At 41 she took a different post as a typist, but it was only after three years of this that she developed severe pain in the right thumb Tenovaginitis was diagnosed At this time she had already begun to experience stiffness of the whole hand whenever she tried to do her shorthand, and, after an operation had been done to relieve the tenovaginitis, her shorthand became impossible She then became a copy typist Thereafter any attempt at writing produced the pain, cramp, and tremor In 1953, when she was 49, even copy typing produced cramp and pain in the muscles of the right hand, arm, and forearm Soon after, the cramp began to show itself in other similar movements, and when first seen in March, 1954, she had an almost constant spasm of the muscles of the right arm and hand An attempt to write produced a slow and painful exhibition



19th August 1954

The Royal Infirmary
Oxford Road
Manchester.

There was an old man with
a gun who espied an old lady
named Pheasant. She sat on a seat
in the sun and he stared and he
stared most unpleasant

Fig 1—Case 1 specimen of writing before (above) and after treatm

characteristic of writer's cramp She had been treated wi benzhexol hydrochloride without success, had receiv extensive courses of various sedatives, and had been advis to give up her work She had become exceedingly depres and anxious about her condition but was struggling to pe form her duties She subsequently left her work in June, 195 and review in August indicated a general increase in h depression and despondency, and the cramp and spasm the right arm had become continuous

Case 2—A male clerk, aged 31, noticed in June, 1 after 2 years in his present post, which involved writing 4–6 hours each day, that after writing for 5 minutes developed a tired feeling in the hand and forearm with trem On his continuing to write his arm rapidly became s his thumb tensed, his hand tended to turn over and writing became illegible Two weeks' holiday did not prod any change, and treatment with phenobarbitone and ben hexol hydrochloride proved unsuccessful In May, 1 he improved a little spontaneously in that the cramp te to develop after a longer interval and his writing was f legible There had been no discernible change in his perso domestic, or economic circumstances to explain this cha Re examination in August, 1954, showed that he wr slowly, stiffly, and with a tremor, but his writing was rat more legible than when he was first seen There were abnormal neurological signs, and no other movement affected

Methods and Results of Treatment of Writer's Cramp

As already stated, tremor and spasm are the t components of the motor disorder These were assail in the following way For the tremor a metal plate w drilled with nine holes ranging from $^{1}/_{2}$ to $^{1}/_{8}$ inch diameter The patient was required to insert a me stylo, held as a pen is held, into these holes, working fr larger to smaller as each size was successfully negoti Electrical circuits were arranged so that, whenever stylo touched the side of the holes, the patient recei a shock passing from palm to dorsum of the *left* hand

A second piece of training apparatus consisted strips of insulating tape arranged in straight, curv and zig zag patterns upon a metal plate and so dispo as to call for all the fundamental finger and hand mo ments required in writing Again circuits were so devi as to produce an electric shock for the patient sho

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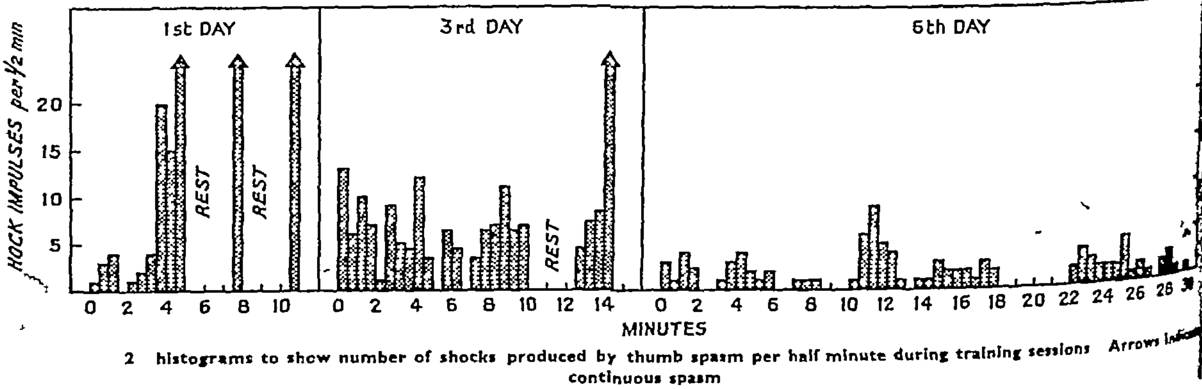
* A further patient has since been treated a man aged 53 with writer's cramp of 2 years duration Six training sessions produced complete cure which has been maintained for 1 month to date



2 histograms to show number of shocks produced by thumb spasm per half minute during training sessions Arrows in continuous spasm

he deviate in any way in tracing the lined patterns with a metal stylo

The third retraining mechanism was an ordinary pen adapted in such a manner that excessive pressure of the writer's thumb would again produce a shock. This device was thus triggered by the spasm component of the disorder in which severe adduction and flexion of the thumb are so prominent.

Case 1.—Treatment was given on 15 successive days, apart from two omissions for Sundays, each session lasting about 30 minutes. The first five sessions were occupied with training on the holes and the tapes. Progress was fitful, but at the seventh session all the holes and the tapes were negotiated successfully, the tremor having disappeared. The next three sessions were spent in writing to dictation with the electrified pen. On the 13th and 14th days writing was almost normal with no evidence of tremor or spasm. On the 15th day she wrote for 15 minutes without effort and considered herself normal. When last seen three months after completion of the course she had maintained the improvement. She has now returned to work after an absence of three months. Fig 1 illustrates her writing before and after treatment.

Case 2.—Tremor was less prominent than spasm in this case. After only two sessions the holes and tapes were overcome and attention was turned to spasm. In six sessions the spasm was abolished and the patient considered himself completely relieved.

Fig 2 illustrates the progress made: it shows in graphic form the frequency per half minute of the sounds made by the shocking coil during writing in the first third and fifth of these sessions. It will be noted that on the first occasion the thumb went into continuous spasm after five minutes writing and that two rest periods did not bring relief. Four months after the end of the treatment this patient is still well and writing normally.

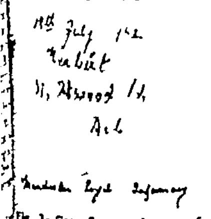

4th July 1952
Tablet
Aberdeen Royal Infirmary

Fig. 3—Case 2: specimens of writing before (above) and after treatment.

Fig 3 illustrates his writing before and after treatment.

Cases 3, 4, 5, and 6 were all male and had had writers cramp for 3–10 years. After 3–5 weeks treatment they have shown degrees of improvement which we have estimated as 50–85% of their previous normal. The patient whose performance is estimated at only 50% considered himself cured and asked to discontinue treatment since his writing was now to him quite adequate. In the remaining cases the impairment of function comprises either a slight tremor or a lack of fluidity in the writing and although one of these patients writes for 7 hours each day in his work as a stockbroker's clerk he does experience some aching in his hand after 3 or 4 hours and so he has been assessed as an 80% improvement.

Typist's Cramp

Case 7.—A female shorthand typist aged 32. In 1949 during a period of domestic stress and after 13 years as a shorthand typist in an accountant's office she began to experience mild cramp in the left hand accompanied by extension of the left forefinger and adduction of the thumb. After 12 months the other fingers began to flex into the palm. In November 1951 she was seen at the Royal Infirmary and psychiatric interviews brought no benefit to her condition. In 1952 she changed her employment, and there was some improvement in her domestic background though there was still cause for anxiety. Her new work was more responsible and more arduous than her former employment and in August 1954 a similar but more painful affection of the right hand developed. After 10 minutes typing the index finger extended the thumb adducted and the remaining fingers flexed into the palm with such force as to produce bleeding if she continued. It was in this state that she returned for further advice.

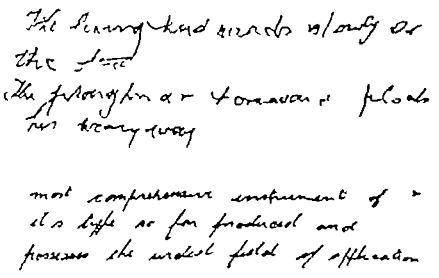

The lowing herd winds slowly o'er the lea
The ploughman homeward plods his weary way
most comprehensive instrument of its type so far produced and possesses the widest field of application

Fig 4—Case 7: specimens of writing before (above) and after treatment.

Treatment and results.—For this case the apparatus was modified so that a small rubber pad was covered with an interweaving pattern of wire connected to the secondary winding of the induction coil. This pad was then fixed into the palm of the patient's right hand. Thus, any flexion of the fingers into the palm caused a mild shock. The patient was then instructed to type. In three sessions of twenty minutes duration on successive days a complete cure was achieved and has been maintained for 6 weeks.

Discussion

Although it is too early to be certain about the long term effects of treatment certain preliminary conclusions seem permissible in the light of these experiences. It is encouraging from the clinical point of view to have evolved a means of alleviating a condition which so often has proved intractable. One feels that in the event of relapse retraining may be of value, but this remains to be seen. Apart from this the physiological and pathological implications of the results of this form of treatment are of interest. We suggested above that the acquired motor skill of writing was susceptible to disorganisation by a process of conditioning and that irrespective of the initial cause of the disturbance the conditioned reflex would continue to operate making normal writing impossible. This heuristic approach to the problem led to the evolution of the method of treatment which really amounts to the extinction of the conditioned reflex which is disorganising the normal pattern of skilled volitional activity. The outcome of this technique of "deconditioning" as it may be called in patients who differed so much in mental and emotional constitution appears to afford support for our view of the physiological mechanism underlying writer's cramp. Further observation and experiments with the remaining patients are proceeding after which it may be possible to advance more definitive conclusions.

As regards the technique of treatment it may be suggested that the apparatus merely represents a symbol or a focus for psychotherapy. This suggestion is difficult to refute categorically but several of the patients had previously had psychotherapy without benefit and the courses of treatment were arranged so that each patient received treatment sessions from both of us. We feel that this type of therapy can be conducted by anyone with sufficient understanding of the mechanical nature of the disorder to be able to apply the various retraining exercises and that the psychological element in the treatment is relatively unimportant.

The patients were under the care of Dr Fergus R. Ferguson to whom we are further indebted for helpful criticism.

REFERENCES

Critchley, M. (1954) *Proc. R. Soc. Med.* 47, 593.
Culpin, M. (1931) Recent Advances in the Study of Psychoneuroses.
Glover, E. (1949) Psycho-Analysis. London.
Pai, M. N. (1947) *J. ment. Sci.* 93, 68.

ROUTINE PREOPERATIVE CHEST RADIOGRAPHY

ANALYSIS OF 1000 CASES

R E LODER

M A., M B Camb , F F A R C S

CONSULTANT ANÆSTHETIST, PETERBOROUGH MEMORIAL HOSPITAL, NORTHANTS

MASS miniature radiography has shown a small proportion of the public to have undiagnosed pulmonary disease without any specific signs on clinical examination It is therefore advisable to radiograph the chest of every patient admitted for non emergency surgery

The main difficulty about routine chest radiography in the past has been that of expense because 17 × 14 in films cost 3s 8d each When, however, this hospital obtained a 5×4 in radiographic camera, the price of each chest film was reduced to just under 5d With the permission of the consultant radiologist and the willing cooperation of the radiographers and nurses, the following routine was instituted

Routine

Since often the patients were operated on the day after admission, there was no time for the usual procedure of filling in all details on a request form and of receiving a signed report back in the wards To prevent any delay the sister or the nurse admitting the patient to the ward filled in the request form as a "routine preop" The patient was radiographed the same day, and the film was inspected by the radiologist Abnormal findings were communicated immediately by telephone to the anæsthetist and discussed between him and the radiologist, the patient was re-examined, and, if necessary, a decision to postpone operation was conveyed to the surgical department concerned

Analysis

The radiographs were taken between July and December, 1954, and of the 1000 patients in this analysis 447 were male and 553 were female

Age groups

The numbers of cases in the different decades were as follows

Years	0–9	10–19	20–29	30–39	40–49	50–59	60–69	70–79	80 or more
Cases	263	120	111	124	157	97	80	38	10

Proposed Operations

General surgical operations numbered 233, including 43 major abdominal operations

Ear, nose, and throat operations numbered 347, including 189 removals of tonsil and adenoid, 15 radical mastoidectomies, and 29 submucous resections of nasal septa

Gynæcological operations numbered 175, including 24 hysterectomies and 35 pelvic-floor repairs

Orthopædic operations numbered 194, including 6 major operations on the hip and 3 on the spine

There were 44 *ophthalmic* and 9 *dental* operations

Radiographic Findings

Of the 1000 cases radiographed 116 films were reported on as abnormal and 29 operations were postponed

Congenital abnormalities 9 cases Only 1 case was of importance, a large pulmonary conus in a child This case was referred to a cardiological clinic, but no definite diagnosis was made

Thickened pleura and diaphragmatic adhesions 14 cases

Emphysema 7 cases One of these showed a localised emphysematous bullæ

se of, and/or infection in, lung 19 cases 8 of in children and 11 in adults 6 cases were l to be minor, and the operation was eventually arranged Of the 13 major infections or collapses 3 were in cases of carcinoma needing immediate treatment They were given intensive preoperative and postoperative physiotherapy and were operated on under an antibiotic screen, one of them under local anæsthesia. 2 cases were already in the hands of the chest physician, and the operations proposed were part of their treatment. 4 cases had severe collapse and infection, thought possibly to be due to bronchiectasis and were referred 2 to the pædiatric physician and 2 to the chest physician. and the operations were cancelled 1 further pat refused treatment and discharged himself from hospital In the remaining 3 cases, early in the se reports were received too late and the operation d without preliminary treatment These 3 patie developed postoperative respiratory complications responded to treatment, 1 of them needing bronchosc before a lower lobe re expanded

Tuberculosis 35 patients were reported as hav healed calcified primary complexes, or calcified foci w no evidence of recent disease, or calcified hilar glan One of these was a child aged 7 years with a report "calcified lesions at right apex, probably tuberculous she was referred to the pædiatric physician for investi tion, the operation being postponed until this had b done 7 adults were reported to have pulmonary tub culosis One of these was already known , the 6 n cases were referred to the chest physician for treatme

Cardiovascular disease 19 cases of cardiac enlar ment or of hypertensive cardiac configuration w reported Only 1 of these patients had symptoms a was referred to a physician before the operation was do 5 patients had not only cardiac enlargement but a hilar congestion 4 of these had already been no clinically as being in heart failure, but 1 patient had n These were all referred to the physician, and their fi outcome was as follows 2 were operated on successfu under local anæsthesia , 2 were operated on un general anæsthesia, and 1 of these, who had a leg amp tated for diabetic gangrene, died on the tenth po operative day , and the fifth patient was not operated

Bone metastases in one film a dense opacity in t 4th rib was reported as being possibly a seconda deposit Since the proposed operation was prostate tomy, the pelvis and spine were radiographed, a carcinoma of the prostate was diagnosed

Comment

From this analysis of 100 preoperative chest radi graphs it can be seen that 29 patients had their operatio postponed or cancelled because of disease first found b radiography The discovery of 6 cases of new ad pulmonary tuberculosis alone justifies the taking of the films

The number of abnormal reports correspond reasonab to the figures given by Wachowski (1954), whose se consisted of all admissions to a general hospital America , and he found rather more rarities. Th proportion of new cases of tuberculosis is higher than th found in mass miniature radiography of the genera public (Stalker 1954)

It is a great comfort to the anæsthetist to know th the patient has had his chest radiographed , if a abnormality is found, one can get advice or treat i accordingly *All 3 patients with preoperative pulmona infection notified too late developed severe postoperati pulmonary complications*

I wish to thank the doctors, nurses, and radiographers a this hospital for their help in instituting and continuing th routine , Dr C W Horncastle, consultant radiologist, witho whose help it would have been impossible , and Mr D W Bracey, consultant surgeon, for help in preparing this pap

REFERENCES

Stalker, R (1954) See *Brit med J* i, 1260
Wachowski, T J (1954) *Illinois med J* 105, 14

RESPIRATORY OBSTRUCTION IN ACUTE LEUKÆMIA

V B LEVISON
M B Lond F.F R D.M R T

SENIOR REGISTRAR, RADIOTHERAPY DEPARTMENT
ADDENBROOKE'S HOSPITAL, CAMBRIDGE

RESPIRATORY obstruction is a rare manifestation of acute leukæmia though in chronic lymphatic leukæmia it is relatively common

Barnick (1898) reviewed the early literature dealing with involvement of the larynx and trachea in leukæmia

Goedel (1932) saw a case of acute myeloid leukæmia in which there were massive œdema of the aryepiglottic region and a hæmorrhagic mass in the glottis, and necropsy showed a hæmorrhagic deposit over the whole inner wall of the trachea extending into the main bronchi

Polisso et al. (1953) described a case of monocytic leukæmia in which laryngeal infiltration necessitated an emergency tracheotomy

A case of monocytic leukæmia was seen by Marks (1953) in which a necrotic membrane involved the left tonsil the vocal cords, and the trachea

Israëls (1953) described an interesting case of reticulum-cell reticulosis of leukæmic form in a woman aged 38 her total white-cell count was 2000 per c.mm. and examination of the bone marrow showed large numbers of the same cells A tracheotomy had to be done because a subglottic mass, presumably composed of the same cells, had almost obliterated the trachea.

I report here two cases of acute leukæmia presenting as respiratory obstruction

Case reports

Case 1—A Polish housewife aged 25 was admitted to hospital on April 26 1954 with six days history of dyspnœa and swelling of the face

On examination she was cyanosed and very distressed by dyspnœa, and superior mediastinal obstruction was present with much œdema of the face and neck. Radiography showed an enormous mass of mediastinal glands presumably pressing on the trachea and main bronchi (fig 1) The total white cell count was 16 000 per c.mm (immature cells 0·5%) but the sternal marrow showed acute leukæmia.

Treatment and Progress—Emergency deep X ray therapy was given to the mediastinal glands two opposing fields 20 × 15 cm (half value layer 1 5 mm. Cu.) being used and a dose of 380r was given to the mediastinum in eight treatments spread over nine days Immediate relief of symptoms followed the first treatment and by May 7 when the treatment was completed the patient was breathing normally and the œdema of the face and neck had gone Her total white-cell count was then 6000 per c.mm (immature cells 28 5%) Re-examination of the chest showed complete resolution of the mediastinal mass (fig 2) No further pulmonary symptoms developed The patient was discharged home but had to be readmitted on May 20 with bleeding from the gums and melæna her total white-cell count then was 22 000 per c.mm (immature cells 68%) She was treated with 6 mercaptopurine and cortisone but did not improve and died on June 4 1954

Case 2—A salesman aged 33 first noticed dyspnœa while cycling in August 1954 and said he felt "his breath was sticking in his throat. Soon after this he had spasmodic swelling of the face and neck and cyanosis. He was admitted to hospital unconscious on Oct 29 1954

Fig 3—Case 2: tomogram showing narrowing of trachea from above clavicles to an inch above carina.

On examination he was breathing stertorously and there were signs of obstruction of the superior vena cava with gross œdema of the face and neck and congested neck veins He regained consciousness after four hours having been given oxygen Radiography of the chest showed in the superior mediastinum a large mass compressing the trachea just above its bifurcation and tomography showed considerable narrowing of the trachea from above the clavicles to one inch above the carina (fig 3) The total white-cell count was 110 000 per c.mm (blast cells 82 5%) The diagnosis of acute leukæmia probably lymphatic was confirmed by examination of the sternal marrow

Treatment and Progress—Emergency X ray therapy was given to the superior mediastinum and trachea two opposing fields 15 × 15 cm. (half value layer 1 5 mm. Cu) being used and a total central dose of 200r was given in three treatments spread over five days. Immediate relief of the respiratory obstruction followed with disappearance of the symptoms of obstruction of the superior vena cava Re-examination of the chest showed considerable diminution of the mediastinal

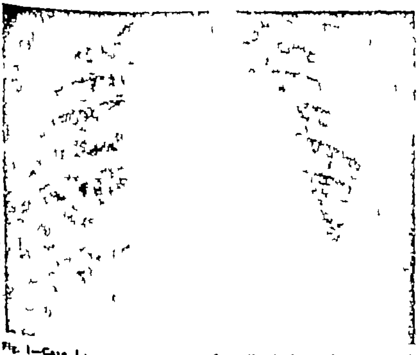


Fig. 1—Case 1: enormous mass of mediastinal glands presumably pressing on trachea and main bronchi.

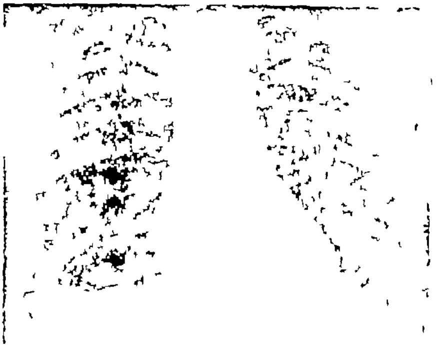


Fig 2—Case 1: complete resolution of mediastinal glands after radiotherapy

glands, disappearance of the mass in the trachea, and establishment of a normal airway The patient has not developed any further symptoms of respiratory obstruction. He is being treated with 6 mercapto purine, and his general condition and blood count are satisfactory

Discussion

In the initial stages of acute leukæmia the lymph glands are not always palpable, though in the later stages of acute lymphatic leukæmia they may be obviously enlarged The condition in which there are an infiltrating lymphosarcoma and a leukæmic blood picture may be termed leucosarcoma, and the two cases reported here come into this category

Sternberg (1915) first described leucosarcoma and considered that it differed from leukæmia and from lymphosarcoma, but this view is not held now (Whitby and Britton 1953) In a series of cases of acute leukæmia reported by Hrodek (1953) only 10% were characterised by swellings, in this group were seen cases showing swelling of the mediastinum, tumour like infiltration of the skin, and multiple infiltrations of various organs It is of considerable importance to distinguish, by examination of the blood and sternal marrow, between cases of leucosarcoma and of lymphosarcoma involving only one group of lymph glands, because the prognosis in leucosarcoma is hopeless, whereas in lymphosarcoma the five-year survival rate is 50% (Boden 1951)

Acute respiratory obstruction due to malignant disease, most often carcinoma of the bronchus, is one of the few radiotherapeutic emergencies Immediate treatment, though not curative, will usually give instant relief from imminent suffocation and death It is generally accepted that radiotherapy is contra-indicated in acute leukæmia (Whitby and Britton 1953, Paterson 1953), but in leucosarcoma presenting with acute respiratory obstruction radiotherapy seems to be of considerable value and may relieve the obstruction and make tracheotomy unnecessary in cases involving the larynx, such as those reported by Poinso et al (1953) and Israels (1953) Leucosarcoma is an extremely radiosensitive tumour, and only very small doses of X rays must be used The response to radiotherapy is very rapid, and the treatment must be given with much care and stopped as soon as the symptoms have been relieved

Summary

Two cases of acute leukæmia presenting as respiratory obstruction are described

In each case complete and permanent relief of the obstruction followed small doses of X rays

The importance of distinguishing between unifocal lymphosarcoma and leucosarcoma is emphasised

Radiotherapy is usually completely contra-indicated in acute leukæmia, but it will relieve respiratory obstruction in this disease, it must be given with the greatest caution

I should like to thank Prof J S Mitchell, F R S, for permission to publish and for helpful criticism, Sir Lionel Whitby, Dr L C Martin, and Dr A. P Dick for permission to publish, Dr F R Berridge for the radiographs, and Miss Sylvia Westoby for printing them

REFERENCES

Barnick O (1898) *Münch med Wschr* 45 589
Boden, G (1951) *Brit J Radiol* 24 404
Goedel, R. (1932) *Arch Ohr Nas, u KehlkHeilk* 132 24
Hrodek, O (1953) *Čas Lék ces* 92 1292
Israels M C G (1953) *Lancet* ii 526
Marks, M. M. (1953) *J int Coll Surg* 20 750
Paterson R (1953) The Treatment of Malignant Disease by Radium and X Rays London p 439
Poinso R Picard, D, Perrimond G Bondil, J N, Bonnet, P (1953) *Sem Hôp Paris,* 29, 4040
St[illegible] C (1916) *Beitr path Anat* 61 75
[illegible] E H, Britton C J C (1953) Disorders of the Blood

INTRA-ARTERIAL TRANSFUSION IN DIABETIC COMA

R M Kalbag
B Sc, M B Bombay
SENIOR HOUSE OFFICER, DEPARTMENT OF NEUROLOGY, FRENCHAY HOSPITAL, BRISTOL

J M Naish
M A, M D Camb, F R C P
CONSULTANT PHYSICIAN, BRISTOL CLINICAL AREA

Surgeons used to dealing with severe states of shock following massive hæmorrhage and tissue damage have quickly come to realise the value of intra arterial transfusion in resuscitating the nearly moribund patient whose systolic blood-pressure has dropped below 70 mm, Hg Because intravenous transfusion of blood has little effect in restoring a normal circulation in such cases, the term irreversible shock has often been used in the past

Intra-arterial transfusion has also been used with success for severe shock in medical conditions, such as cardiac infarction and various types of embolism. We record a case of diabetic coma in which peripheral circulatory failure had reached a stage which would in the past have been considered irreversible, and in which an intra arterial transfusion of two pints of blood was the turning point towards eventual recovery

Case-report

A woman, aged 63, not previously known to be diabetic, who had complained of anorexia and constipation for two months, began to vomit profusely thirty six hours before admission She became drowsy and finally comatose twelve hours before admission

On examination she was obese but extremely dehydrated, with respirations deep and hungry, extremities cold temperature 97°F, and blood pressure 80/60 mm. Hg Her urine contained glucose and acetone Her blood sugar level was 463 mg per 100 ml, and bicarbonate 19 5 vol %

Treatment and Progress —She was given 25 units of soluble insulin intravenously and 75 units intramuscularly, and intravenous therapy was started with physiological saline solution 400 ml A blackish foul gastric residue was aspirated. After two hours the blood sugar level had risen to 800 mg per 100 ml and the blood pressure had fallen to 50/25 mm. Hg Insulin 160 units was given, and intravenous dextran was substituted for the saline solution Venous spasm, persisting after the injection of procaine, prevented very rapid transfusion, and signs of pulmonary œdema began to appear five hours after the start of treatment At this time the blood sugar level was 650 mg per 100 ml and the blood-pressure 55/40 mm Hg The patient was cold and livid, her breathing was stertorous, and the end seemed imminent. A pint of blood was then transfused into the right radial artery in ten minutes, the general condition improved, and the blood pressure rose to 100/65 mm Hg A further pint was then given in five minutes, with a further improvement in general condition An hour after the beginning of intra arterial transfusion the blood pressure was 115/75 mm Hg and the patient's extremities were warm Intravenous therapy was continued through a polyethylene catheter in the left saphenous vein, 2 litres of 1/6 *M*/sodium lactate and ¾ litre of physiological saline solution being given in four hours Insulin 60 units was given at hour eight, and at hour ten the blood sugar level was 246 mg per 100 ml Thenceforward treatment was continued with sodium lactate, physiological saline solution, and potassium chloride intravenously according to the estimated needs, and insulin was given four hourly After twenty four hours the patient was just able to swallow fluids, and, although for two more days her condition was critical and recovery was complicated by sepsis at the sites of the intravenous and intra arterial transfusions by urinary infection, and by a recurrence of iritis in one eye, she has eventually been stabilised on 70 units of insulin zinc suspension ('Lente')

Comments

In the experience of one of us, such a degree of peripheral circulatory failure in diabetic coma always presages death, and accelerating the rate of intravenous infusion, even if that is possible, seems to precipitate pulmonary œdema Intra arterial transfusion although an unusual method of treatment seemed to offer the only hope of halting the cycle of events leading to circulatory failure and death

The transfusion was effected with a Hamilton Bailey cannula tied into the radial artery just above the wrist and connected to a form of pressurised-saline outfit on a stand which has been in regular use in Frenchay Hospital Bristol since 1948 mainly for angiography principally carotid (Mortimer and Gaskell 1954) Alternative routes, perhaps preferable from the point of view of maintenance of continuity of the artery would be either percutaneous introduction of a 6 in B W G no 17 needle into the femoral artery or direct puncture of the brachial artery at the elbow after exposure The use of a Macintosh and Pask safety drip chamber excludes the possibility of air-embolism but the blood has to be prefiltered, no filter being provided with the apparatus

REFERENCE

Mortimer P L., Gaskell K H (1954) *Brit J Radiol* 27 535

HYPERSENSITIVITY ANGIITIS

REPORT OF A CASE

J R Edge
M.D Leeds M.R C P
CONSULTANT PHYSICIAN

S Fazlullah
M B Osmania D T.M & H
MEDICAL REGISTRAR

J Ward
M.B Lpool, D C P
ASSISTANT PATHOLOGIST

NORTH LONSDALE HOSPITAL BARROW IN FURNESS LANCS

Since Kussmaul and Maier (1866) first described periarteritis nodosa this term has been used to describe various conditions the common factor being a generalised arteritis or angiitis varying in type and distribution

Numerous cases of periarteritis have been attributed to sensitisation to drugs—e.g sulphonamide (Rich 1942, More et al 1946) sulphathiazole (Lichtenstein and Fox 1946) thiouracil (McCormick 1950) thiourea (Gibson and Quinlan 1945), penicillin (Surdakowski 1951 Adelson 1951) organic arsenicals (Miller and Nelson 1945), dilantin aspirin and Lugol's iodine (Rich 1947); and the resulting lesions which differ in some respects from those of classical periarteritis nodosa have been called hypersensitivity angiitis (Zeek 1952 Knowles et al 1953) We have not been able to trace any reference to hypersensitivity angiitis following the administration of streptomycin or of isoniazid

Another important group of cases of periarteritis nodosa is often associated with hypertension and renal impairment and has been called microscopic periarteritis nodosa (Davson et al. 1948, Wainwright and Davson 1950)

Additional descriptive terms used for members of this group of diseases include polyvasculitis (More et al. 1946) primary and secondary periarteritis nodosa allergic granulomatous angiitis, rheumatic arteritis temporal arteritis (Zeek 1953) polyarteritis nodosa and necrotising arteriolitis (*Lancet* 1954)

The importance of a better understanding of these diseases has recently been emphasised (*Lancet* 1954), particularly because a possible means of treatment is now available in corticotrophin and cortisone The present case is reported as an example of hypersensitivity angiitis in which death occurred suddenly during treatment with cortisone

Case report

Mrs A a housewife was treated in 1951 at the age of 30 for a sterile mammary abscess which *settled completely* a few days after incision a chest radiograph at that time was normal

She remain well until April 1954 when she developed suppurative otitis media which was treated with systemic penicillin This had to be discontinued after a few days because of fever and a general rash shortly after this she developed right sided pleuritic pain which persisted On May 20 1954 radiography of the chest showed two dense homogeneous rounded opacities in the lower zone of the right lung one 2 cm in diameter lying at the anterior end of the greater fissure and the other (6 cm. in diameter) lying posteriorly in the costophrenic sulcus (fig 1)

She was first seen by one of us on June 24 when the right pleuritic pain had been worse for the past few days. She was found to have a small right pleural effusion and she was admitted to hospital the same day The effusion was clear and contained lymphocytes, but no tubercle bacilli were found on direct examination or culture The diagnoses considered at that time included secondary carcinoma tuberculomata pyæmic abscesses, and infarcts. In the absence of any evidence of a primary carcinoma a course of anti tuberculosis chemotherapy was started the intention being to proceed to thoracotomy if the diagnosis remained in doubt The effusion cleared in two weeks leaving the diaphragm considerably raised and subsequently the rounded lesions were not radiologically visible

Course of Illness

Treatment with streptomycin 1 g daily and isoniazid 200 mg daily was started on June 28 On July 4 she had fever (102°F) and a general maculopapular rash, which she said was exactly like what she had had after treatment with penicillin. The pyrexia increased and on July 6 streptomycin therapy was discontinued and full doses of promethazine (Phenergan) were given Isoniazid therapy was not discontinued until July 8 The *pyrexia which had remained at* 104–105 F until July 8 gradually settled to about 100°F; at this time there was eosinophilia (594 per c.mm.) which was not maintained

By July 10 the rash had largely cleared but on the 14th she developed acute retention of urine requiring an indwelling catheter; at the same time all the tendon jerks were brisk those in the right leg being much increased The plantar responses were flexor and the abdominal reflexes present; there were no sensory changes. Her general condition remained poor drowsiness being a striking feature; the *skin of the* legs had started to desquamate The blood pressure was 115/70 mm. Hg and blood urea level 22 mg per 100 ml

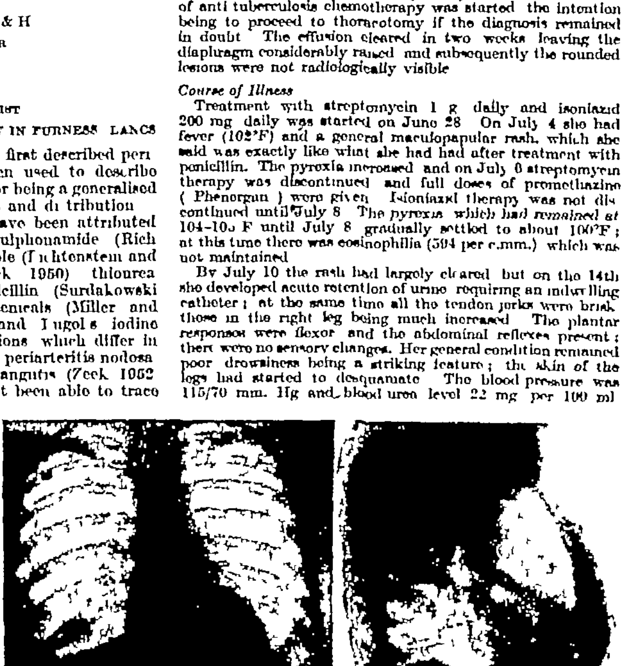


Fig 1—May 29 1954: two dense homogeneous rounded opacities in lower zone of *right lung* one lying at anterior end of greater fissure and the other posteriorly in costophrenic sulcus.

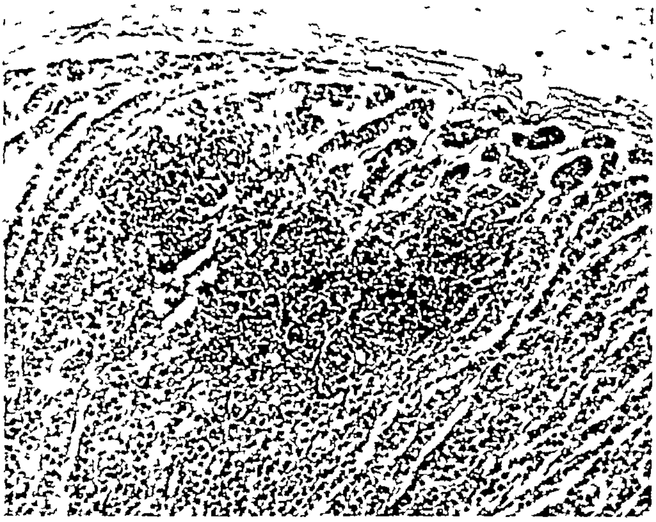


Fig 2—Necrotic area in suprarenal cortex (× 77¹/₂)

The right fundus oculi was normal, but there were two well defined patches of exudate on the nasal side of the left disc, there was one perivascular exudate on the temporal side of the disc but no hæmorrhage or papillœdema

On the evening of July 14 she had signs of a pulmonary embolism in the left lower lobe, apparently arising from thrombophlebitis in the left calf Anticoagulant treatment with heparin and phenylindanedione ('Dindevan') was started but had to be stopped after twenty four hours because of gross hæmaturia

All drugs were now discontinued, and the patient gradually improved Extreme drowsiness remained the chief feature of the clinical picture By July 26 the neurological signs had completely regressed, and micturition was normal, but slight desquamation was now general

On Aug 10 a test dose of intramuscular streptomycin 0 1 g was followed by mild evening pyrexia (99 2°F) and next day by aching finger joints and back for a few hours On Aug 13 a test dose of isoniazid 20 mg was followed by evening pyrexia (100°F) and next day by severe bilateral conjunctivitis, and the pyrexia subsequently gradually increased to 102 4°F The eye condition progressed and presented a picture indistinguishable from phlyctenular conjunctivitis due to sensitivity to tuberculo protein, a Mantoux test, with 1/1000 O T was negative Drowsiness increased, and the patient complained of stiffness in all her joints

Treatment with Corticotrophin

Polyarteritis being suspected, treatment with corticotrophin 100 mg daily was started on Aug 19 The following day the temperature returned to normal, and the eyes, though still injected, were very much improved The dosage of corticotrophin was reduced after two days to 75 mg daily, and after another two days to 50 mg daily On Aug 23 the patient's condition again deteriorated with pyrexia (101°F) and a relapse of the eye signs Next day treatment with cortisone acetate 25 mg six hourly by mouth was started and continued until Aug 30, no corticotrophin being available During this period she was maintained on a low salt diet and her intake of fluids was restricted to two pints daily

On Aug 29 she complained of breathlessness and retrosternal tightness, and on auscultation there were abundant râles throughout both lungs On the 30th the blood-urea level was 300 mg per 100 ml, compared with 22 mg two weeks previously The blood pressure was 120/80 Electrocardiography showed no abnormality other than prominent T waves, presumed to be associated with the uræmia Radiography of the chest showed diffuse shadowing in keeping with pulmonary œdema The symptoms became worse, and the patient produced copious pink frothy sputum She died on Aug 31

Necropsy Findings (Sept 1)

External examination showed an operation scar below the right breast and some exfoliation of the skin of both legs. A little free fluid was found in the left pleural cavity Both lungs had firm dark red areas at the bases with overlying fibrinous pleurisy, the rest of the lungs being œdematous. The myocardium was pale, otherwise no cardiac abnormality was found The kidneys were swollen and had pale mottled cortex The spleen was moderately enlarged, firm, and pale at the surface, with perisplenitis The liver was somewhat pale The other organs appeared normal to the naked eye.

Histological Examination

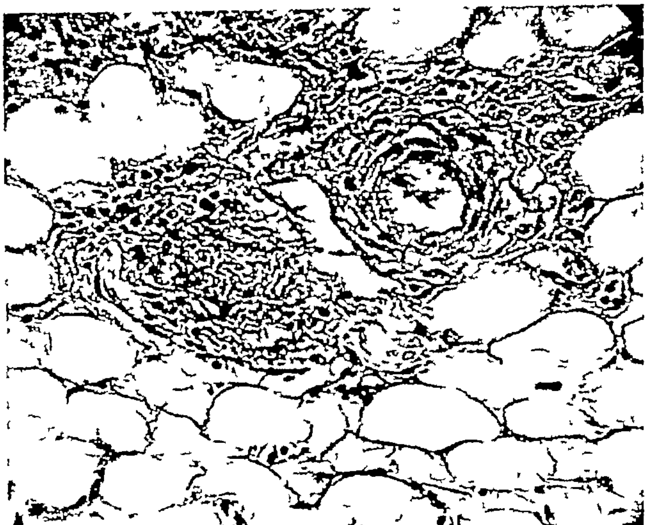
Kidneys —Widespread fibrinoid necrosis of the glomerular tufts, with polymorph infiltration around the capsule. Many tubules contained hyaline and leucocytic casts and red blood cells The interstitial tissue showed round cell and polymorph infiltration No evidence of arteritis was seen in any of the larger vessels examined

Lungs —There were numerous areas in which the alveoli contained fibrin, red cells, and polymorphs, the arteries in these areas being involved by polyarteritis There was no evidence of tuberculosis or of pulmonary sepsis

Suprarenals —Small areas of necrosis in the cortex of both glands (fig 2), no involved vessels were seen in the gland substance, but several were affected in the surrounding fat including a small vein (fig 3)

Small arteries in the *heart* (fig 4), *spleen*, and *portal tr* were affected

The lesions corresponded in nature and distribut to those described by Zeek (1952) as hypersensitiv angiitis, and, except for the involvement of a sm



ected arteriole and vein in perinephric fat (× 244)

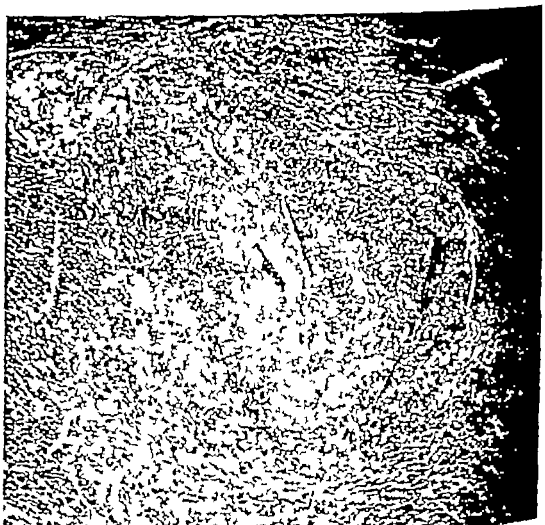


Fig 4—Affected coronary artery (× 25)

tein to those described by Davson et al (1948) as microscopic periarteritis nodosa

Discussion

We now believe that the round opacities seen in the right lower zone of the chest radiograph in April 1954, were due to infarcts and postulate that arteritis had already developed probably as a result of sensitisation to penicillin in March 1954 Subsequently this condition appears to have been aggravated by the exhibition of other antigens in the form of streptomycin and isoniazid after a tentative but mistaken diagnosis of tuberculosis It was not until the patient had recovered from the more usual effects of sensitisation to these drugs (pyrexia, exfoliative dermatitis, and hyperreflexia) and developed a progressive and obscure illness following exhibition of single small test doses that a collagen disease was suspected.

She was then treated with corticotrophin and later cortisone but after two weeks, during which her clinical condition improved somewhat she developed acute fatal cardiorenal failure At no time was the blood pressure raised

Zeek (1952) suggests that, since periarteritis nodosa and malignant hypertension have been produced in rats by the administration of either adrenal or pituitary hormones it may be dangerous to use cortisone or corticotrophin in cases with certain types of necrotising vascular lesions. Rich et al (1950) in experimental work on rabbits in which periarteritis nodosa and glomerulonephritis were induced by sensitising them to horse-serum found that whereas corticotrophin prevented the development of the renal lesions cortisone, in contrast, induced a severe hæmorrhagic type of glomerulonephritis which was distinct from the proliferative variety resulting from sensitisation

More recently several workers have described instances where periarteritis nodosa was possibly caused by treatment with these hormones

Levin et al. (1953) reviewing 50 patients with rheumatoid arthritis treated with cortisone and corticotrophin mention 3 who developed histologically proved periarteritis nodosa (1 during treatment and 2 shortly after treatment with the hormones was withdrawn) They point out that other collagen disorders may coexist with rheumatoid arthritis (Bauer et al. 1952)

Robinson et al (1953) describe 4 patients with rheumatoid arthritis who developed diffuse arteritis, of whom 3 had been treated with corticotrophin and 1 had not.

A similar case of polyarteritis nodosa developing during cortisone treatment of rheumatoid arthritis is described by West and Newns (1953)

Corticotrophin has been incriminated as the cause of serious or fatal allergic reactions

H. T Howat cited by Savidge and Brockbank (1954) and Hill and Swinburn (1954) each report a fatality following injection of corticotrophin due to anaphylaxis

Nabarro (1954) remarks on the danger of allergic reactions to corticotrophin particularly where the adrenal glands fail to respond and the level of circulating steroid hormones is low

Stoner and Whiteley (1951) found that the adrenals of 4 patients who died under treatment with corticotrophin were hypertrophied whereas those of 3 patients who died under treatment with cortisone were atrophied and inactive Whereas the diseases being treated with corticotrophin were sufficient to account for death, those being treated with cortisone were not The adrenals of the present patient who received both hormones for only short periods showed numerous small areas of necrosis

We offer no explanation for the course of events in the case we describe but we believe that the possibility that the patient became sensitised in turn to the hormones, with further aggravation of the generalised angiitis cannot entirely be ruled out The experimental work of Rich and his associates suggests that in the present state of knowledge patients with any form of polyarteritis should be treated with corticotrophin rather than cortisone in view of the possible nephrotoxic action of the latter hormone

Summary

A case is described in which generalised hypersensitivity angiitis developed evidently as the result of sensitisation to penicillin streptomycin and isoniazid

Death took place suddenly from acute cardiorenal failure during treatment with cortisone

Our thanks are due to Mr H. C Taylor for the photomicrographs

REFERENCES

Adelson, L (1951) *J Pediat* 39 346
Bauer W., Ginzler, A. M., Kulka J P (1952) The Protean Nature of the Connective Tissue Diseases Rheumatic Diseases Philadelphia
Davson J Ball J Platt R. (1948) *Quart J Med* 17 175
Gibson, I C Quinlan J T (1945) *Lancet* ii, 108
Hill B H R. Swinburn P D (1954) *Ibid* i 1218
Knowles H C jun, Zeek, P M Blankenhorn M. A (1953) *Arch intern Med* 92, 789
Kussmaul A. Maier R (1866) *Dtsch Arch klin Med* 1 484
Lancet (1954) ii 693
Levin M. H., Rivo J B Scott W, Figueroa W G Frod L. Barrett T F (1953) *Amer J Med* 14, 265
Lichtenstein L Fox L J (1946) *Amer J Path.* 22 665
McCormick, R V (1950) *J Amer med Ass* 144 1453
Miller H. G Nelson M. G (1945) *Lancet* ii 900
More, R. H McMillan, G C., Duff G L. (1946) *Amer J Path* 22 703
Nabarro J D N (1954) *Lancet* ii 1101
Rich A R (1942) *Bull. Johns Hopk. Hosp* 71 123
— (1947) *Harvey Lect* 42 106
— Berthrong M. Bennett I L. (1950) *Bull Johns Hopk Hosp* 87 549
Robinson W D French, A J Duff I F (1953) *Ann rheum Dis* 12 323.
Savidge, R S, Brockbank W (1954) *Lancet*, ii 893.
Stoner H B, Whiteley, H J (1951) *Ibid* p 892
Surdakowski, A Z. (1954) *N Y St. J Med* 54 388.
Wainwright, J, Davson J (1950) *J Path Bact* 62 189
West, H F., Newns, G R. (1953) *Lancet*, ii 1123
Zeek P M (1952) *Amer J clin Path* 22 777

CONGENITAL DIAPHRAGMATIC HERNIA
IN A PREMATURE INFANT

C L. Clinton Thomas
F.R C.S
SURGICAL SPECIALIST MALAYAN MEDICAL SERVICE

Early diagnosis and immediate surgical intervention are largely responsible for the progressive decline in the mortality from congenital defects of the diaphragm. At one time surgical opinion favoured postponing the operation until the child was 1 or 2 years old but Hedblom (1925) showed that three quarters of these infants died before the end of the first month

In the last decade it has been established that during the first 48 hours of their life infants can withstand major surgical procedures which they will *not* tolerate later The early operation has the added advantage that, during the first 2 days of life, the intestines are not yet distended with gas and repositioning is easier This is a serious problem in congenital diaphragmatic hernia because the capacity of the abdominal cavity is considerably reduced

In infants who are operated on after the first 2 days replacement of the viscera and closure of the abdominal wall if possible at all gives rise to serious cardiorespiratory embarrassment which often proves fatal Ladd and Gross (1940) were the first to advocate a two stage closure of the abdominal wall in certain cases and this proved an important advance in treatment

Other important causes of the progressive decline in mortality have been the segregation of these cases in pædiatric and thoracic surgical centres improved techniques in anæsthesia, and the better understanding of preoperative and postoperative treatment in neonatals.

Several large series have now been reported including those by Hartzell (1940) Harrington (1948) Gross

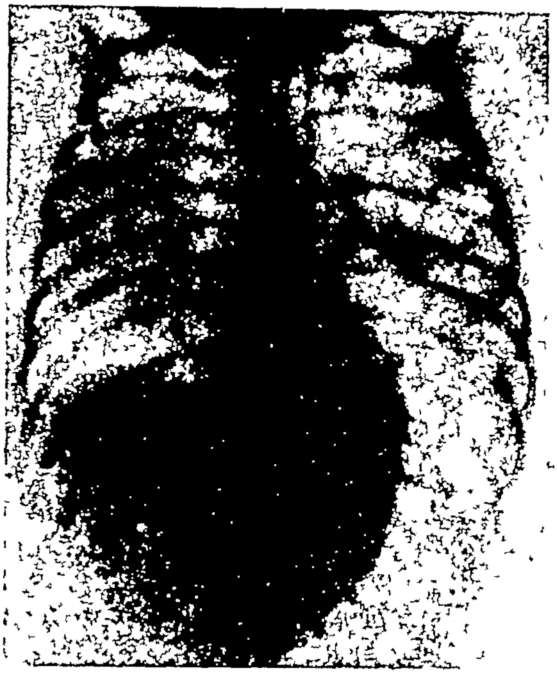


Fig 1—Radiograph of chest before operation

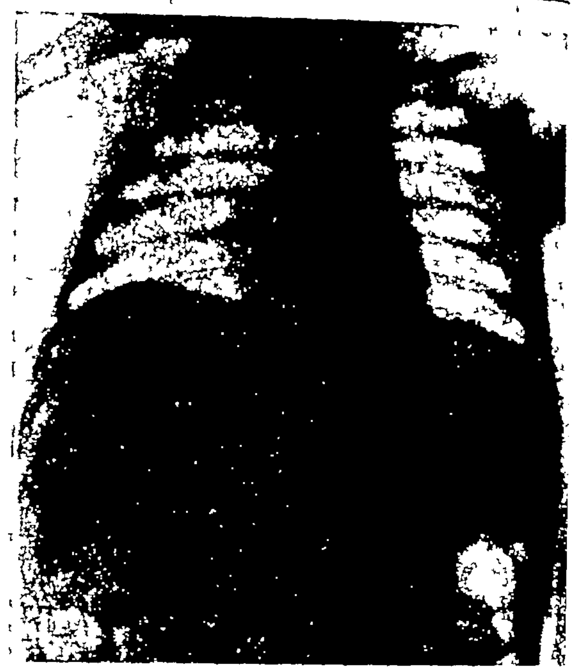


Fig 2—Radiograph after operation

(1953), and Ricker (1954) My justification for recording a single case only is that it shows that success is possible in a poor-risk subject, in the absence of modern anæsthesia and specialised nursing This may encourage surgeons who work in parts of the world where such important aids to surgery are not available

Case-report

A premature male Indian infant, who weighed 4 lb 8 oz at operation, was noticed to be cyanosed on the third post natal day The cyanosis progressively increased, and the infant began to have attacks of respiratory embarrassment and vomiting during feeding Despite these ominous signs a careful examination was not made, and penicillin was given empirically for what was thought to be a respiratory infection Though there was no improvement in his condition, the chest was not radiographed till the twelfth day The film revealed a diaphragmatic hernia with many loops of gas filled intestine filling the left hemithorax (fig, 1) The infant was accordingly referred for surgical treatment

On admission he was cyanosed, dyspnœic, and dehydrated The apex beat was in the right anterior axillary line, and the abdomen was scaphoid.

Dehydration was corrected with subcutaneous half normal saline given through a drip with the aid of hyaluronidase, and gastric suction was begun

Operation

After a left phrenic crush, the abdomen was opened through a left paramedian incision extending from the costal margin to below the umbilicus Anæsthesia consisted in local infiltration of the line of the incision with 1% procaine and adrenaline 1 in 500,000, very small amounts of ether were given, using an open mask, with oxygen supplied through an intranasal catheter

The hernia was through the patent left pleuroperitoneal canal—the so called foramen of Bochdalek The hernial contents were gently reduced after air had been admitted to the pleural cavity through a soft rubber catheter As is usual in this type of hernia, there was no sac

The organs which had herniated were the left lobe of the liver, the stomach and first part of the duodenum, the jejunum, the ileum, the cæcum, ascending colon, transverse colon, the tail and body of the pancreas, and the spleen It was at once apparent that it would be impossible to replace all these viscera in the underdeveloped abdomen A two stage reduction was therefore decided upon

The hernial orifice was repaired in two layers with mattress of fine braided nylon, without preliminary paring phragmatic edges As the last suture was being tied, air was evacuated from the pleural cavity through a fine catheter attached to an abdominal sucker

The skin and subcutaneous tissues at the sides of the abdominal incision were widely undermined As much of the bowel as possible was returned to the abdomen, and the rest was left under the sutured skin as a ventral hernia

Postoperative Progress

At the end of the operation the infant's condition was fairly satisfactory He was placed in an incubator and remained there for 5 days Gastric suction and subcutaneous fluids were continued for 24 hours, when feeding with expressed breast milk was begun. Penicillin 100,000 units twice daily and ascorbic acid 250 mg daily were given postoperatively

As the infant's condition remained completely satisfactory and a radiograph of the chest showed full expansion of the left lung (fig 2), it was decided to repair the ventral hernia on the 7th day However examination of the abdominal wound on that day showed a moderately severe wound infection, though there was no pyrexia (A swab from the wound subsequently grew a penicillin insensitive *Staphylococcus aureus*) Operation was postponed and the wound treated with 5% chloramphenicol in propylene glycol, while chloramphenicol palmitate (100 mg 8 hourly) was given by mouth

The wound infection had cleared up by the 14th postoperative day, and 2 days later the ventral hernia was repaired and the abdominal wall closed in layers

Recovery from the second operation was uneventful and the wound healed by first intention The infant was discharged from hospital 3 weeks later, by which time he was gaining weight normally Subsequent progress was satisfactory, but when the child was last seen, a year later, radiographic screening showed that the left diaphragm was raised, and paradoxical movement indicated that the paralysis had not recovered.

Comment

Ladd and Gross (1940) originally advised preliminary crushing of the phrenic nerve to decrease tension on the diaphragm caused by suturing the opening Healing takes place satisfactorily without this aid, and Gross (1946) has since abandoned the procedure because—as in this case—the paralysis of the diaphragm is sometimes permanent

REFERENCES

Gross, R E (1946) *Amer J Dis Child* 71 579
— (1953) Abdominal Surgery in Infants and Children. Philadelphia
Harrington S W (1948) *Surg Gynec Obstet* 86, 735
Hartzell, J B (1940) *Amer J Surg* 48, 582
Hedblom, C A. (1925) *J Amer med Ass* 85, 947
Ladd W E, Gross R. E (1940) *New Engl J Med* 223, 917
Ricker, W L (1954) *Arch. Surg* 69, 291

Reviews of Books

The Physician and His Practice

Editor JOSEPH GARLAND M D editor *New England Journal of Medicine.* Boston and Toronto Little Brown. 1955 Pp 270 $5 00

IN this 'source book of information regarding his career for the young doctor in the United States, 18 contributors (13 medical, 5 lay-expert) survey the whole field of medical practice—opportunities obligations, rewards, and perils, and give detailed advice on all except clinical matters to the intending general practitioner For the British reader its interest lies in comparison. It seems that fragmentation of medicine has gone further there even than here so that general practice in cities has become something very different from ours. In small towns and the country however the generalist' may fully deserve that title besides having his part to play in vigorous and abounding social and communal life Graduation to special through general practice still occurs, and group practice of various kinds is increasing In one respect the American G P scores heavily: it seems to be recognised that wherever he may practise he must in some way be affiliated to a hospital, "since he will stifle medically without it. "Perhaps Dr Garland comments, a way will be found to modify the present scheme in Britain and give the general practitioners some access to hospitals. It would seem a safe assumption that if this is not done the caliber of general practice is likely to deteriorate in time.

Hey Groves's Synopsis of Surgery

Editor SIR CECIL WAKELEY BT K.B.E C.B LL.D., F.R.C.S senior surgeon King's College Hospital, London. Bristol: John Wright & Sons. 1954 Pp 660 30s

THERE is a great deal to be said for this synopsis, and when an ordinary treatise of surgery has been read and re-read. For revision in the last month or so before an examination, and as a companion at outpatient clinics and round the wards it is invaluable Its merit resides in its ultimate degree of terseness a treatment may be summarised in a single word capable of recalling a memory It saves the student from re-reading what he already knows, but forces him back to his textbook for what he has forgotten Students owe a debt of gratitude to Sir Cecil Wakeley for editing this new edition

X ray Atlas and Manual of Esophagus, Stomach and Duodenum

Dr T J J H MEUWISSEN consulting physician and radiologist at Eindhoven, The Netherlands. Amsterdam and New York: Elsevier London: Cleaver Hume 1955 Pp 687 £8 15s

IN the introduction to this work we are told that material for it has been gathered from twenty five years experience in gastro-intestinal radiology Nearly 500 cases are described briefly and are very well illustrated This mass of clinical material would have made the book difficult to read if the author had not adopted the method he has done: after a comparatively short and very practical survey of the anatomical arrangement and diseases in different regions he groups the illustrative cases as a block The illustrations are of course keyed to the text so it is possible to use them as references either independently or in conjunction with the text A short appendix deals with the stomach after operation No attempt has been made to include references to published works. This is a very helpful book and well produced

Management of Endocrine Disorders of Menstruation and Fertility

GEORGEANNA SEEGAR JONES M D assistant professor of gynecology Johns Hopkins University Springfield Ill Charles C Thomas. Oxford Blackwell Scientific Publications. 1954 Pp 108 42

THIS book is written for the medical student and physician be he specialist or practitioner : but it is better suited to be a primer for student endocrinologists The pituitary and gonadotrophic hormones have certainly been called by many different names and are assayed in many different ways by many different workers, but nine-tenths of these early confusions might have been relegated to an appendix, or at least to footnotes. Here and there the clinician will prick up his ears, hoping to learn something to his advantage but the imprint of clinical experience seems to be lacking A discussion on delayed menarche, for instance, gives the impression that imperforate hymen is high on the list of causes. Treatment of the menopause is dismissed in only one short page; the suggestion that stilbœstrol should be given in doses of 1 mg daily is not likely to commend itself to most recipients and the reader, having been advised that œstrogen treatment must be discontinued as rapidly as possible is then told that ' pellet implantation is most satisfactory when feasible '

Psycho chirurgie et fonctions mentales

J LE BEAU Paris Masson 1954 Pp 430 Fr 3300

IN this book Dr Le Beau a neurosurgeon who has worked particularly in the field of psychosurgery reviews the practice of cerebral surgery in mental illness, including intractable painful states.

After a brief section on the anatomy and physiology of the frontal lobes and their related structures in the thalamus, diencephalon and brain-stem, he discusses, mainly in terms of Eysenck's theories of ' neuroticism and psychoticism, the psychological functions involved in the mental diseases treated He goes on to describe his own experience and gives details of the operative techniques he uses and their possible surgical and medical complications The main part of the book is taken up by a review of the indications for the different operations and their clinical results both in mental disease and for the treatment of intractable pain. This section contains a full discussion and assessment of Dr Le Beau's own results in which postoperative psychological changes have been assessed by Mrs. A. Petrie. There are also brief chapters on temporal lobe surgery in conduct disorders and on the placing of selected lesions in the subcortical nuclei of thalamus and basal structures by means of the *stereo-encephalotome.* In a final chapter on physiological interpretations there is perhaps a tendency to assign rather naively symptomatic changes to specific cortical areas and cerebral structures.

In general however this work covers psychosurgery more fully than many earlier books, which have tended to deal largely with one operation, and surgeons will find it a valuable source of reference

Manual of Hand Injuries

H MINOR NICHOLS M D., clinical instructor in surgery University of Oregon Medical School Portland Chicago: Year Book Publishers London: Interscience Publishers. 1955 Pp 352 72s

WELL illustrated and attractively presented this book provides a complete picture of the problems arising in the treatment and care of injuries of the hand—including amputations, burns tendon and muscle injuries nerve injuries, fractures, and dislocations It also deals with infections secondary tendon repairs, and more complicated reconstructive procedures. The text indicates the tendency towards more serious study and care of hand injuries and the trend in the better hospitals to make the casualty department rather more than a reception station It is a treatise that is of the greatest value to surgeons concerned with the treatment of such injuries, and can be strongly recommended

The Origins and History of Consciousness

ERICH NEUMANN Translator: R F C HULL. London: Routledge & Kegan Paul 1954 Pp 493 30s

FROM any reader not familiar with the Jungian modes of thought and language this book demands steady concentration an unlimited capacity to digest abstractions, and a considerable tolerance for ponderous and imprecise argument If he can bring these rare attributes, he will be rewarded by many unusual and stimulating connections that are suggested between the primitive or archetypal phases of the development of consciousness in individuals and the mythological symbols and tales which are projections of the collective unconscious of mankind The work is essentially an esoteric study in individuation; it seeks to relate ontogenesis to phylogenesis As always in Jung's analytical psychology, the apparatus of scholarship is fully deployed, and the writer shows a wide acquaintance with ancient religious and ethnological writings, especially those concerned with the ubiquitous symbol of the Uroboros—"the circular snake, the primal dragon of the beginning that bites its own tail" Cursory exposition of the way Dr Neumann develops his theme is impossible, because of the unconventional line of thought and the range of issues traversed

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Abdominal Operations (3rd ed London H K Lewis 1955 Pp 1580 £8 10*s*)—Mr Rodney Maingot's work has an established place in British surgical literature, and the third edition has broadened its scope There are now 24 contributors, 8 from overseas, chosen for their expert knowledge in a special subject, and a detached and reasoned approach to each topic is maintained throughout, with ample references The number of illustrations has been increased considerably The revision required for this edition must have been a considerable undertaking, but it has been well worth while

Cold Injury—The Josiah Macy, jun, Foundation, New York, has published the transactions of the conference on this subject held in February, 1954 The editor is Dr V. Irené Ferrer (1955 Pp 226 $4 50)

Technique and Significance of Œstrogen Determinations—The proceedings of a conference on this subject held by the Society for Endocrinology and the endocrinology section of the Royal Society of Medicine in February, 1954 have been published as no 3 of the Memoirs of the Society for Endocrinology The editors are P Eckstein and S Zuckerman Beginning with this number, the Memoirs are being published by the Cambridge University Press, from which copies of Memoirs 1–3 can be obtained (1955 Pp 95 18*s*)

New Inventions

A RULER FOR USE IN ELECTRO-ENCEPHALOGRAPHY AND ELECTROCARDIOGRAPHY

THE measurement of frequency of waves, occurring in short bursts in electro-encephalograms, with a centimetre ruler is tedious and not alleviated by the wave analyser, which analyses epochs of ten seconds To make such measurements easier a ruler has been designed to measure frequency and amplitude of waves The same ruler can also be used for measuring intervals in seconds and cycles per minute so that it is possible to analyse an electrocardiogram displayed on plain paper The ruler is simple to make and does not require the skill of an instrument maker This is important because the dimensions of the ruler are determined by the paper speed of each instrument

The ruler is made by etching lines on a piece of 'Perspex' 8 cm × 12 cm × $^1/_8$ in A triangle is etched whose base is 6 cm (or the distance moved by the paper in 2 sec) and vertical height 10 cm The base is divided into six equal parts, and the divisions are joined to the apex of the triangle From the two lines adjacent to the vertical, horizontal lines are etched towards the edge of the ruler, the ones on the right indicating cycles per second (C P S) and those on the left indicating fractions of a second In etching the scale markings, the distance, in centimetres, from the apex of the triangle (measured along the vertical) to the scale markings is calculated as follows

(1) *C.P.S* Distance =

$$\frac{\text{C.P.S represented by 1/6 base (3)} \times \text{vertical height (10)}}{\text{C P S on scale}} = \frac{30}{\text{C P S on scale}}$$

(2) *Seconds* Distance =

$$\frac{\text{Vertical height (10)} \times \text{seconds on scale}}{\text{Seconds represented by 1/6 base (1/3)}} = 30 \times \text{seconds on scale}$$

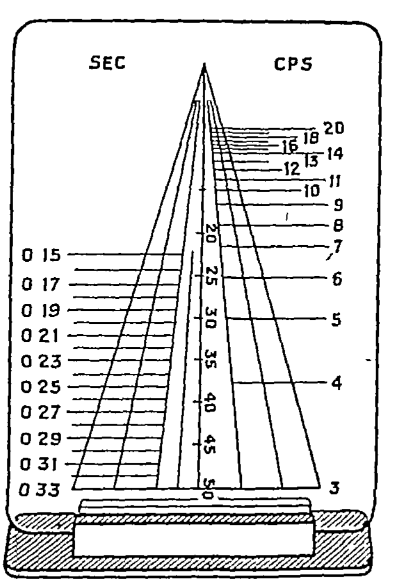
The *vertical line is* marked in centimetre divisions

When the base of a wave is cut by the vertical and the line adjacent on the right, its frequency can be read from the C P S scale on the right Similarly, when the vertical and the line adjacent on the left are used, the duration of the wave or interval can be read on the seconds scale on the left Should lines other than those immediately adjacent to the vertical be used, the figures representing C P S and seconds are doubled or trebled Alterations can also be readily made when the paper speed is halved or doubled

When the sides of the triangle cut similar points in two cardiac cycles in the electrocardiogram, the cardiac rate is read on the C P S scale and the number multiplied by ten This is obvious when it is remembered that the base represents 2 seconds—i e, 30 C P M.

The ruler can be used in such a way that the vertical line of the triangle lies along the base of a series of waves The ruler is then moved to the right or left until one of the lines above the vertical cuts the apex of the wave to be measured The point on the vertical line where this occurs indicates the voltage of the wave depending on the calibration of the instrument (in the present case 1 cm is equivalent to 50 µV)

It is an advantage to etch an additional line midway between the vertical and the line adjacent on the left because this allows intervals of short duration to be measured When this additional line is used, the numbers on the seconds scale are, of course, halved



It is strongly recommended that the ruler when not in use should be supported on a base so that the perspex *is not scratched*

Some tips for the amateur instrument maker are as follows

(1) When the lines are etched with a ruler and needle, the sheet of perspex should be laid on a sheet of carbon paper

(2) An angle poise lamp enables the light to be directed at an angle most convenient for showing up *the lines.*

(3) When the lines are etched they should be rubbed with carbon paper, and the excess wax removed with a cloth. This makes the lines appear black against white paper

(4) Vertical lines raised *outside the* limits of the ruler on the sheet of perspex avoid unnecessary and unsightly marks on the ruler itself

(5) A vibrator tool is useful for etching the numbers. The numbers, of course, must be printed in reverse because the etched surface of the perspex ultimately forms the under surface of the ruler

Voltage markings on the vertical, in multiples of 5 for convenience, can be calculated as follows

Distance, in cm, from the apex to the voltage marking =

$$\frac{\text{(mV or } \mu\text{V on scale marking} \times 30\text{)}}{\text{(Distance moved by paper in 1 sec)} \times \text{(mV or } \mu\text{V equiv to 1 cm)}}$$

STEWART RENFREW
M.R.C.P

ISOBEL HAGGAR

E.E G Department,
Royal Infirmary,
Glasgow

THE LANCET

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Society and the Criminal

> " a crime should never be divorced from the background or setting in which it occurs if it is, then the situation is prejudiced and judgment becomes distorted "

In saying this in the course of his Morison lecture to the Royal College of Physicians of Edinburgh last year[1] Sir **David Henderson** was drawing a close and interesting parallel between the clinical manifestations of nervous and mental illness and the behaviour and thought disorders indicating abnormality and crime

> "They stem he said from the same sources they start early, they are psychobiologically determined are characterised by clinical manifestations which are closely akin, are susceptible to similar methods of investigation and are most successfully treated at a preventive level.

Moreover, as he pointed out in an earlier passage, the responses of society to them are much alike For centuries it was customary to treat brutally patients suffering from acute recoverable forms of mental disorder 'their incurability was manufactured " In a like manner crime has always stirred us to retaliate 'The cry for revenge is hearty and spontaneous ' Insanity still evokes in many people a revulsion not explicable at the conscious level and the aggression evoked by crime has similar obscure origins It is as though these things were infectious breeding in us irrational and antisocial responses which we are not immediately able to recognise for what they are Perhaps it would be truer to say that they rouse uneasy recollections of the same forces in ourselves, forces held perhaps precariously, in check and our automatic defence takes the form of cruelty we would strike down the messenger who brings us evil tidings of our inner selves

The ætiology of criminal behaviour like that of mental illness he believes is complex and cannot be pinned down to a single cause such as environmental stress It must include not only parental attachments but constitutional factors—hereditary developmental endocrine, and metabolic Separation from the mother in the early years may indeed be one such factor but can hardly be the only one in fact criminal behaviour he suggests is not a symptom but a reaction type—a social reaction type if you prefer it but still a psychobiological reaction dependent on our particular make up, however it may have been forged This might seem to hark back to **Lombroso** were it not that Sir **David** allows as much weight to environment as to constitution and has moreover a humane concern for the criminal as a person. He sees him as dominated ("like every other individual) by emotional storms and distorted ideas which may stem from his unconscious life "and which under certain circumstances may be completely uncontrollable" He notes, too, that delinquency, like mental instability, often manifests itself for the first time at puberty and he mentions how closely some older criminals resemble paranoiacs in that starting from wrong premises, they build up a more or less logical argument which is as unshakeable as the systematised delusions of paranoia

Many such people have come under his observation for since 1921 his psychiatric opinion has been sought on criminals whose nervous or mental stability was suspect at trial Before 1932 the cases sent to him were nearly always of murder or attempted murder but since then all manner of behaviour disorders have been referred—cases of theft housebreaking sex offences, fire raising and others He takes this change to indicate a growing alliance between the law and medicine which in time may lead to a better behaved society He classifies 477 cases referred to him under names given of old to three of the seven deadly 'sins lust (*150 cases*), *malice* (*171 cases*), *and greed* (*156* cases) The 150 criminals convicted of crimes of lust ranged in age from 12 to 80 years and came from all walks of life They included 4 cases of bestiality 8 of sodomy 8 of incest, 5 of rape 5 of obscene letter writing 33 of homosexual conduct and 87 of lewd conduct The striking thing about this group as a whole—more astonishing to laymen, however than to doctors—is the high proportion of the criminals who were of normal mentality as assessed by intelligence tests only 12% were diagnosed as insane, 17% as mentally defective and 17% as psychopathic while over half (54%) were 'sane ' in the sense in which the public and the law use the term

> The distribution of the sane (in this sense) in the six subgroups is interesting Thus of the 4 guilty of bestiality none could be classed as sane whereas of the 8 guilty of sodomy all could but that is not to say Sir **David** comments, that they were not strange abnormal individuals who were driven by strong instinctive impulses and desires which became overmastering Of the 8 people guilty of incest, 6 ranked as sane and 1 out of 5 of those guilty of rape could be so classed ; whereas 5 writers of obscene letters were all suffering from paranoid states
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> All 33 of the homosexuals fell into the sane group Nearly all of them were of high professional standing—schoolmasters clergy Civil Servants, bankers, lawyers and the like Many said they would not change their emotional inversion even if they could but a few were desperately anxious for help

Sir **David** comments regretfully on the inconsistency of the sentences passed on homosexuals which ranged from one to three years imprisonment Where medical treatment seemed likely to be of use the judge often said that whatever medical treatment was needed would be given in prison The effect of imprisonment of course is to confine the homosexual for long periods to the society of his own sex and perhaps to confirm him in his inversion Sir **David** did not make this criticism though doubtless he had it in mind He holds, as do most doctors nowadays that homosexual tendencies most probably depend on a failure to develop and mature the patient remaining fixed at a homosexual level Our aim, he suggests must be to gain the confidence of the legal profession and persuade them to accept this concept This is not easy to do he points out in view of our lack of success in the treatment of homosexuality , but he might perhaps have drawn the analogy of a leg which ceases to grow people neither blame the doctor because he cannot always start the growth process off again, nor abuse the patient for having a limp

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[1] Society and Criminal Conduct Edinburgh The Royal College of Physicians 1955 Pp 41

> The 87 lewd-conduct cases formed the largest subgroup under the heading of lust, and varied from exhibitionism to interference with young children Only 29 of them were intellectually normal 11 of them were insane, 22 mentally defective, and 26 psychopathic Their oft-repeated offences were often precipitated by alcohol

SIR DAVID remarks on the incurability of these cases, whether treated in a mental hospital or a prison , and on the difficulty of reconciling legal and medical opinion on them Here again we are dealing with a developmental disaster—with people who have reached neither emotional nor instinctual maturity, even though they may " wear the mask of sanity " Sometimes they detest their aberrations as violently as anyone else (as seems to have been the case with the prisoner recently sentenced for assaulting two policewomen [2]) the criminal who is aware of a disorder in himself which society does not recognise as such is not uncommon, and must suffer greatly The 171 crimes of malice included murder, attempted murder, assault, child neglect, threatening letters, and fire raising SIR DAVID found 43% of these criminals insane, and 13% mentally defective or psychopathic (as against only 12% insane and 34% defective or psychopathic among those convicted of crimes of lust)

> Murder is often the solitary crime of a person who otherwise has had a good record, and where there are mitigating circumstances the convicted murderer is often reprieved, and usually makes a satisfactory social adjustment, never committing another offence

The 156 crimes of greed included 122 of theft and 34 of fraud As with crimes of malice, more than half the criminals were insane (33%) or mentally defective (16%) or psychopathic (6%) persons Among those guilty of fraud were some criminals of ability who combined a paranoid personality with an obsessive need to show off , and these, he found, were the most difficult to influence of all criminal types

Abnormality and unsoundness of mind, SIR DAVID HENDERSON argues, cannot be accepted as synonymous , for many criminals are abnormal in that they have failed to fit into ordinary social life, without showing any " unsoundness of mind " which could be certified as such according to existing definitions In this opinion he differs, as he points out, from NORWOOD EAST and HUBERT, who believed that " the normal group of offenders constituted at least 80% of the receptions " He is well aware that the criminals he classes as abnormal, whether sick or not, may be a danger to society, and he recommends that in all cases of serious crime, when the accused's life-history shows evidence of malignant trends, detention should be indeterminate—as it is with certified mental patients Discharge should depend on the attainment of social responsibility This is an extension of the idea of the indeterminate sentence now being tried in Denmark and of the indefinite sentence which is on trial here Finally he urges the great need for more intensive investigation of character traits, so that we may in time be able to distinguish their diagnostic and prognostic significance Forensic psychiatry would then be in a position to point to particular clinical and psychobiological reactions, whether dependent on genes or derived from the environment Such research might also put our profession in a stronger position to convince the lawyers of a concept now generally accepted by doctors—namely, that a person can at one and the same time be intellectually mature and emotionally and instinctually immature that the " sound mind " cannot, in fact, be measured in terms of intellectual performance alone

Valvotomy for Pulmonary Stenosis

THE results of valvotomy for simple pulmonary stenosis are extremely encouraging CAMPBELL and BROCK [1] review 58 cases treated in this way at Guy's Hospital, London 25 of these patients were cyanosed at rest, and a further 7 were thought to become cyanosed with exercise The sex-distribution was almost equal The majority were between the ages of 5 and 29, but 5 were over 30 , and 3 cyanosed children were operated on at 4 years of age Of the 8 deaths associated with the operation 5 were in the first cases , since then there have been 3 deaths in 52 cases Cyanosis betokens increased risk , of the 8 deaths only 1 was of a patient who was not cyanosed As CAMPBELL and BROCK remark, in cases where cyanosis has appeared the best time for operation has been passed The 50 survivors have been followed for or more years (the longest for six) and none has Only 4 patients were not improved In nearly all of the remainder improvement was considerable , for example, a cyanosed woman gave birth to a child eleven months after valvotomy and can now walk as far as she pleases, whereas previously she was limited to a hundred yards In the cyanotic group improved colour and exercise tolerance were observed clinically , but only half of the acyanotic patients showed any disability, and improvement had often to be judged by objective methods alone CAMPBELL [2] suggests that, in the absence of symptoms, the clearest indications for valvotomy are cardiac enlargement, electrocardiographic evidence of right ventricular strain, and a right ventricular pressure of 100 or more mm Hg In the series reported by CAMPBELL and BROCK the heart size, measured radiographically, decreased or remained stationary after operation in nearly all patients with enlarged hearts , but in those with small hearts the size commonly increased a little, apparently owing to their greater physical activity In 3 patients the heart enlarged still further, and in 2 of these the clinical result was poor The electrocardiogram improved in 26 of the 31 cases in which there had been evidence of right ventricular strain Inversion of the T wave in leads V_{1-5} disappeared or decreased considerably , the changes usually began about six months after operation and continued for up to three years The 5 patients in whom the electrocardiograms showed no change included 3 who did not improve clinically, but the remaining 2 have so far done well Cardiac catheterisation was repeated in 24 patients after operation , the right ventricular pressure had fallen to less than half the former figure in all, and to a third in some, and in many the pressure gradient across the valve had diminished remarkably Arterial oxygen saturation was invariably improved in cyanosed patients, in all but 2 the interatrial shunt was abolished and the polycythæmia decreased accordingly

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[2] Times May 10 1955

[1] Campbell, M Brock R *Brit Heart J* 1955, 17, 229

[2] Campbell M *Ibid* 1954, 16 273

This series is the largest yet described in detail **Hosier** et al,[3] whose results seem very similar have reported 89 cases in summary **Blount** et al[4] have described a small series of 15, in 5 of which valvotomy was done through the pulmonary artery under hypothermia In these 5 patients the right ventricular pressure was reduced to normal, but pulmonary regurgitation developed in at least 4 This has always been feared as a hazard of pulmonary valvotomy but it was observed only 3 times by **Campbell** and **Brock** and in only 1 patient was it serious While it may seem disappointing that after operation the right ventricular pressure does not fall to normal **Campbell** and **Brock** feel that it is preferable for the surgeon to leave behind mild stenosis than to produce severe regurgitation by attempting too much So far no patient with a good result has begun to deteriorate again, but only further observation will show how long the improvement lasts The operative risk is not large and the mortality is likely to be reduced by submitting patients to valvotomy as soon as the need becomes apparent

Annotations

ULCER-CANCER OF THE STOMACH

In his Macewen lecture Prof Matthew Stewart has once more raised the topic of ulcer-cancer in the stomach[5] Examination of 1510 specimens removed surgically showed a combination of chronic simple ulcer with carcinoma in 103 and coexistence of the two lesions in a further 13 Simple ulcer was present in 935 cases. This might suggest that the proportion of simple ulcers which become cancerous is about 10% but as Stewart observes many gastric ulcers heal spontaneously so in fact the ratio must be lower For other reasons too it is difficult to assess the incidence of ulcer cancer Gastric carcinoma is more commonly situated in the pyloric region than on the lesser curve in the ratio of about 3 to 1 whereas for simple gastric ulcer the ratio is reversed Since patients with a simple prepyloric ulcer are liable to come to *operation* earlier owing to earlier complications than those with a similar lesion on the lesser curve the material from surgical specimens can hardly be regarded as a random sample Similarly with cancer pyloric lesions are diagnosed earlier and operated on earlier the fact that cancer of the body is more often removable and is therefore more likely to provide specimens adds a bias in the opposite direction but it is unlikely that these two considerations neutralise one another

Beattie and Moroney[6] approached the problem statistically in an attempt to prove that in the stomach an association between simple ulceration and cancer does exist but because of errors of sampling in existing evidence they were unable to do so Ivy,[7] approaching the problem experimentally, has examined the possible action on gastric mucosa of carcinogens—overheated fats certain food dyes and methylcholanthrene He concludes that water-soluble agents may incite malignant change directly but those insoluble in water can produce malignant degeneration only in the presence of a chronic ulcer or gastritis since secretion of mucus and epithelial desquamation protect the mucosa adequately This work indicates possible explanations of ulcer-cancer but provides no proof.

STANDARDISATION OF WOUND TEXTILES

Most wound dressings are applied to protect the injured surface from contamination and to absorb exudate For these purposes gauze and if the secretions are copious cotton wool are commonly used Baron[1] has compared in laboratory animals the mortality and the rate of wound healing with different dressings Where the wound was superficial, healing was more rapid if the raw surface was exposed to the air With deeper wounds, dressings produced better results Absorption of secretions varied considerably with different types of textiles. When absorption was poor the secretions spread beneath the dressing infection occurred and the mortality increased With thicker dressings and a more closely woven fibre improved absorption was associated with poor central evaporation and the persistently wet dressing resulted in wet infected wounds

Ideally fabric for wound dressing should not adhere to the tissues At present, the only non adherent materials are impregnated in a way which destroys their powers of absorption The fabric should be close woven, and should not swell greatly on wetting or shrink on drying—changes which greatly retard wound healing The finishing of the textile is important matting with titanium oxide and brightening with optical whiteners are often the cause of wound irritation

TREPONEMAL AGGLUTINATION TEST

The immobilisation test for *Treponema pallidum* (T.P I test) is at present the only practical specific test for the serodiagnosis of syphilis.[2] This test is technically difficult and considerable experience is required to read the reaction correctly The technical difficulties include the need to avoid using sensitised spirochætal antigens the deterioration of the survival medium used, the toxic action on the living treponemes of some sera and the anticomplementary action of other sera which may invalidate the test In addition there is always the danger that laboratory workers may be infected by the living organisms These difficulties can be largely overcome by the creation of special units but this is expensive and it draws away from general laboratories workers who can often ill be spared Accordingly this test has been restricted to a few specialised laboratories.

For many years investigators have attempted to evolve a simple specific agglutination reaction In 1953 McLeod and Magnuson[3] described their experiences with a treponemal agglutination (T P A) test *T pallidum* killed either by the antiformin method of Tani or by heat and oxophenarsine hydrochloride yielded satisfactory antigens On the other hand, formalin killed *T pallidum* did not agglutinate in the presence of syphilitic serum while phenol killed organisms showed some spontaneous agglutination McLeod and Magnuson found that the addition of fresh steer serum accelerated and enhanced agglutination and that the reaction was complete after two hours incubation at 37°C They concluded that the results of this test compared favourably with those of the T P I test both in specificity and sensitivity

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[3] Hosier D M, Pitt J L, Taus ig H B World Congr Cardiol. Washington 1954 p 242

[4] Blount S G Jun McCord M C Mueller H Swan H Circulation 1954 10 161

[5] Ulcer-Cancer of the Stomach By Matthew J Stewart C.B.E., M.D. LL D F.R.C.P. F.R.F.P.S Glasgow Jackson for the University 1955 Pp 31 5s.

[6] Beattie A D Moroney M J *Brit J Cancer* 1952 6 315

[7] Ivy A C *Gastroenterology* 1955 28 315

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[1] Baron H *Nature Lond.* 1955 175 60

[2] See *Lancet* 1954 ii 1165

[3] McLeod, C Magnuson H J *Publ Hlth Rep Wash.* 1953 68 747

Hardy and Nell[4] have lately reported their work on agglutination of *T pallidum* by sera from rabbits and human beings with treponemal infections Unlike McLeod and Magnuson they do not employ steer serum The technique is simple but requires eighteen hours' incubation at 37°C after mixing the antigen and serum Hardy and Nell conclude that the natural treponemal infections of rabbits and the close immunological relationship of these infections to syphilis explain the spontaneous clumping of the organisms in suspensions of *T pallidum* They also suggest that the more superficially placed antigen of *T pallidum* reacts with Wassermann reagin, whereas the deeper somatic antigen reacts with the specific treponemal serum agglutinin If this is so, the specificity of the standard tests for syphilis (S T S) will have to be re examined These workers use heat in the preparation of their antigen, but as a further precaution the sera to be examined are absorbed by S T S antigen before the agglutination test is done In addition they use ethylene-diamine tetracetate to overcome the inhibitory action of a divalent cation which is normally present in human serum They conclude, as a result of testing 430 human sera, that this relatively simple test has a specificity comparable to that of the T P I test and considerably greater than that of the S T S

Dardoni[5] tested the technique of McLeod and Magnuson and concluded that, because of auto-agglutination of the organisms in the suspension of *T pallidum*, it could not yet take the place of the T P I test Price and Boxall,[6] in this country, after a preliminary investigation of the technique of Hardy and Nell suggest that more research is required before it can be used routinely Nevertheless, it would seem that this type of test holds great promise

TUBERCULOUS PLEURISY

THORACIC surgeons have provided pathologists with material for studying almost all stages of pulmonary tuberculosis from the primary complex to the chronic cavity Good use has been made of the opportunity, as is evident from Medlar's[7] detailed monograph Lately pathologists have also been examining specimens from patients with tuberculous pleural effusions

Stead et al[8] describe 24 cases in which the chest was explored within a few months of the beginning of symptoms All the patients were thought to have tuberculous effusions, and tubercle bacilli had been recovered from half of them Thoracotomy was done because there were features in each case that "did not completely conform to the usual clinical picture" In fact, half were found to have non-tuberculous effusions, although in 3 of these acid-fast bacilli had been reported in sputum or pleural fluid 15 were tuberculous, and the pleural sacs were removed with varying amounts of lung tissue In 12 there was a caseous lesion in the lung just beneath the diseased pleura In almost all of these 15 the pleura itself was more than 1 cm thick and contained pockets of liquid caseous material In 7 all segments of the lung had many small nodules which were not apparent in the preoperative radiographs The clinical results are said to have been excellent in 12 of the 15 ; in 2 the decortication was inadequate, and in 1 staphylococcal empyema developed

Stead et al emphasise that it is not their policy to explore all cases of "idiopathic" pleural effusion They state that 10 of the 24 patients were operated on to remove the residual thick pleura , and their description of the removed pleura might certainly suggest that this tuberculous tissue was better out than in But none of the patients had been observed for longer than thirteen months after onset of symptoms , and it is well known that the pleura has astonishing powers of healing, and that all but a few patients without demonstrable lung lesions will remain well Wynn-Williams and Shaw[9] found a five year relapse rate of 15% in 128 patients, only 14 of whom were given antibacterial treatment, and Emerson[10] observed no relapse in 17 patients treated with antibacterial drugs and followed for two years

Not all would agree that the risk is so small In this country the five year relapse rate was long supposed to be about 30% But Roper and Waring[11] have recently reported reactivation of tuberculous disease in no less than 92 (65%) of 141 young men in the five years after a pleural effusion had developed while they were serving in the U S Armed Forces It is generally agreed that pleural effusions in young adults are almost always tuberculous and very seldom, if ever, "idiopathic", and that whatever may be the extent of the risk the condition should not be treated lightly But it is very doubtful whether surgical extirpation can play a useful part

OCULAR OCHRONOSIS

IN 1948 Anderson[12] first reported a new ocular syndrome in industrial workers engaged in the manufacture of hydroquinone Miller[13] has described in detail a small group of cases in this country In this syndrome the cornea and conjunctiva are stained in the area of the palpebral fissure The cornea has a brown sepia-like stain which traverses the whole thickness of its substance and in severe cases may seriously impede vision There are other changes which interfere with accurate vision—namely, vertical folds in Descemet's membrane, a white precipitate within the corneal substance due to protein denaturation, deformation of the anterior surface of the cornea producing irregular astigmatism, and in some cases ulceration In the early stages the conjunctival changes consist in drying and thickening in the palpebral fissure, and this area later becomes yellow Finally discrete dark patches develop over the white of the eye in the palpebral fissure on either side of the cornea, separated from it by a clear area Once the corneal staining has appeared, there is likely to be permanent visual disability , this is not alleviated by contact lenses, but might conceivably be reduced by corneal grafting The conjunctival staining gradually disappears without ill effect

There seems little doubt that the main cause of this syndrome is lengthy exposure to the vapour and dust of quinone—an intermediate product in the manufacture of hydroquinone Where the eye is protected by goggles or where the process is enclosed, the ocular changes do not arise There is some slight evidence that long continued exposure to an atmosphere heavily polluted with hydroquinone dust may produce corneal ulceration if the worker is unhygienic and careless in his protective habits , but some men have worked for twenty years in such an atmosphere without any change appearing As far as is known, there has never been an instance of this syndrome in workers who handle hydroquinone during photographic development

The clinical picture of this syndrome is of theoretical interest because it is almost identical with that of alkaptonuria and carbolic poisoning The ætiological link is the staining of the eye either exogenously or endogenously by a salt of hydroquinone For this reason the three conditions have been grouped together under the name ochronosis—a word coined by Virchow[14] who first described the pathological findings in alkaptonuria and wished to distinguish the disorder from melanosis

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[4] Hardy P H jun Nell E E *J exp Med* 1955 101, 367
[5] Dardoni L *Riv Ist sieroter ital* 1954 29, 440
[6] Price, I N O , Boxall B B Personal communication
[7] Medlar E M *Amer Rev Tuberc* 1955, 71, no 3, part 2 See *Lancet* May 21 1955 p 1063
[8] Stead W W Eichenholz, A Stauss H *Amer Rev Tuberc* 1955, 71, 473
[9] Wynn Williams N Shaw, J B *Tubercle* 1955 36, 74
[10] Emerson P A *Quart J Med* 1955 24, 61
[11] Roper, W H., Waring J J *Amer Rev Tuberc.* 1955 71, 616
[12] Anderson B *Arch Ophthal , Chicago* 1948, 38 812
[13] Miller, S J H *Trans Ophthal Soc U K* 1954, 74 349

THE CAUSE OF POSTURAL PROTEINURIA

A FEW weeks ago we said that the mechanism of postural proteinuria was still unknown[15] An important contribution has since been made by Greiner and Henry[16] These workers criticise the view[17] that the proteinuria is directly due to increased pressure in the inferior vena cava and renal veins, and refer to an experimental study[18] in which increase of caval pressure to 150–220 mm saline, maintained for thirty minutes, caused no proteinuria

Carefully controlled observations in six young men with postural proteinuria indicated that the most important ætiological factor is pooling of blood in the extremities. Advantage was taken of the fact that postural proteinuria is particularly liable to occur in hot conditions[17] and all the observations were made at a temperature of 122 F Lordosis in the supine position produced proteinuria once only whereas venous-occlusion cuffs applied at a pressure of 80 mm Hg to all four limbs resulted in proteinuria in all the subjects Proteinuria, which regularly occurred after tilting the subjects to a 70 head up position was prevented by compression of the legs, which effectively inhibited peripheral pooling of blood

Greiner and Henry point out that their observations explain the facts that postural proteinuria is commoner in hot conditions producing peripheral vasodilatation and in motionless standing[17] which is particularly liable to cause pooling of blood in the legs They suggest that deviation of blood from the heart and lungs causes arterial vasoconstriction which is proportionately greater in the renal arterial system The erect lordotic posture greatly reduces the renal plasma flow[19] but this fall is no greater in cases of postural proteinuria than in non proteinuric controls.

LUNG CANCER IN ASBESTOSIS

THE causes of cancer of the lung are probably mainly exogenous[20] but each of the definitely known carcinogenic substances—e.g ores in Schneeberg and Joachimstal mines bichromates—accounts for only a minute proportion of all cases. Doll[21] now confirms suggestive evidence that lung cancer is an occupational hazard of asbestos workers Examination of the cause of death in 105 persons who had been employed in one asbestos works showed that 18 had had lung cancer associated in 15 cases with asbestosis The mortality of 113 men who had worked for at least twenty years in places exposed to asbestos dust was compared with the mortality experience of the whole male population There were 39 deaths in the first group whereas 15·4 were expected: the excess was due to deaths from lung cancer (11 compared with 0 8 expected) and from other respiratory and cardiovascular diseases (22 compared with 7 6 expected) The average risk among men employed for twenty or more years has been of the order of ten times that experienced by the general population This risk has become progressively less since the precautions introduced as a result of the Asbestos Industry Regulations 1931 to prevent dust dissemination in the works became effective

Gloyne[22] found in his series of 1205 specimens of lungs with dust diseases including 121 of asbestosis, that the rates for primary neoplasm of the lung in male and female asbestos workers were 20% and 10% respectively Barnett[23] found 31 deaths with carcinoma of lung in 235 deaths associated with asbestosis during the years 1924–46 with a distribution of 17 2% male and 8 4% female deaths Adjustments for length of exposure to the dust and age at death would scarcely account for the discrepancy in the figures between the two sexes The same discrepancy exists in the figures for all cases of carcinoma of the lung Kennaway and Kennaway[24] showed that the rates of female to male deaths in England and Wales had changed from 1 1 9 in 1921 to 1 : 4 0 in 1945 between 1935 and 1945 the increase was 250% for males and 170% for females If the causes of cancer in the lung are the same for both sexes (as in asbestosis and possibly in smoking), can the sex discrepancy be related to the baffling fact that while the total "amount" of tumour in both sexes is approximately equal 40% of the cancer deaths in females are from carcinoma of organs peculiar to the female,[25] leaving correspondingly smaller numbers for other sites? If so, what internal factor determines this organ selectivity?

Unlike asbestosis the main causes of dust diseases in the lungs are not associated with an increase in carcinoma of the lungs and Kennaway and Kennaway[26] showed that bronchial carcinoma is less common in coal workers than in the general population James[27] has confirmed this very neatly by comparing a series of South Wales coalminers with a series of non miners in the same area, obtaining figures of 3 3% for the former and 5 4% for the latter but he points out that the relatively low incidence of tumour in the miners may be partly due to dust disease causing death before the average cancer age The dust diseases generally act on the connective tissues, and there is no satisfactory explanation of why the asbestos fibres should affect the epithelium as well

EPILEPSY AND THE ELECTRO ENCEPHALOGRAM

IMPROVED techniques of electro-encephalography (E E G) have confirmed some earlier correlations of electrical with clinical activity, such as that of bilateral 3-per second wave-and spike patterns with petit mal have led to the modification of some such as that of square topped waves and a sharp down peak with psychomotor epilepsy and have cast renewed doubt on others such as the identification of the cortical spike focus with the site of origin of an epileptic discharge.[28]

Gibbs and his colleagues[29 30] have described valuable information about the natural history of E.E G abnormalities which has important clinical implications By following changes in E.E G patterns as infants and children develop they have obtained a longitudinal section of electrical brain activity to supplement the brief cross sectional view of isolated E.E G recordings They point out that the immature brain tends to react to various possibly epileptogenic traumata with a generalised electrical abnormality Moreover the pattern of reaction differs at different stages of maturation In infancy hypsarhythmia (continuous slow wave high voltage discharge with diffuse spiking) is common, as the first decade of life is traversed, at first "petit-mal variant" (2-per second sharp and slow waves) and then "classical petit mal" (3 per second wave and-spike activity) are more usual In adolescence and adult life the electrical response to cerebral insult becomes more localised This is so with epileptogenic factors occurring ab initio at this age, and may also apply to activity shown earlier as a generalised response in childhood *Focal activity, though less common, does also occur in* childhood, and, unlike the generalised response, it may clear spontaneously or change in form and site as age advances Thus, *occipital foci, present* rather more often in the 1–5 age group, had tended by the age of 9 either to disappear (40%) or to change their location (37%) to a temporal or possibly subcortical site, while midtemporal foci, by the age of 15, had either cleared (54%) or migrated to an anterior temporal or subcortical site (38%)

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[14] Virchow R Virchows Arch 1866 37 212
[15] Lancet May 1955 p 958
[16] Greiner T Henry J P J Amer med Ass 1955 157 1373.
[17] Bull G M Clin Sci 1948 7 77
[18] Farber, S J Becker W H Eichna L W J clin Invest 1953 32 1145
[19] King S E Baldwin D S Proc Soc exp Biol N Y 1954 86 634
[20] Gough, J In Recent Advances in Pathology Edited by G Hadfield London 1953; p 198
[21] Doll, R Brit J industr Med 1955 12 81
[22] Gloyne, S R Lancet 1951 i 810
[23] Barnett, G P Annual Report of the Chief Inspector of Factories for the year 1947 H M Stationery Office 1949
[24] Kennaway E L Kennaway N M Brit J Cancer, 1947 1 260
[25] Kennaway E L Brit med J May 7, 1955 p 1107
[26] Kennaway E L Kennaway N M Brit J Cancer 1953 7 10
[27] James W R L Brit J industr Med 1955 12 87
[28] Meyers R Epilepsia, 1954 3 1
[29] Gibbs E L Gillen, H W Gibbs F A Amer J Dis Child 1954 88, 596
[30] Gibbs E L Fleming M M Gibbs F A Pediatrics 1954 13 66

Gibbs and his school have done a great deal to advance the clinical value of electro encephalography, and these studies put us further in their debt The evidence that some focal abnormalities disappear spontaneously with age will be welcome to all those dealing with epilepsy in childhood It confirms clinical observation and underlines the need for caution in excising "epileptic foci," especially in the young Moreover, the change in focus once more raises the question of whether the primary site of epileptic discharge is cortical Gibbs et al speak of "*migrating foci*," which is a vivid description, but the change may be due to altered activity in one part of a complex neuronal circuit allowing activity already present in another part to emerge more clearly We still know too little of what the E E G pattern represents in terms of cellular neurophysiology

This work has further value in posing many clinical questions We are not told what proportion of those with focal and general E E G abnormalities had focal or general fits, nor is it clear, apart from the statement that "many develop multiple foci," what happens as age advances to the varying forms of generalised abnormality found in childhood Finally we need to find out the proportion of children who show these abnormalities *but have no clinical attacks at all*

GALL-BLADDER AND HEART-BLOCK

CONFLICTING views are held on the relations between the gall-bladder and the heart These fall under three headings—namely, the differential diagnosis between angina pectoris and the pain of gall bladder disease, the coincidence of gall bladder disease and coronary-artery disease in the same patient, and the possibility that gall bladder disease may aggravate existing heart-disease

White and his co workers[1] reported clear evidence of disease of the gall bladder in 6 8% of 1000 patients, who presented clinically with coronary artery disease They found at necropsy that disease of the gall bladder was almost twice as common in patients with severe coronary artery disease as in those with normal coronary arteries This association, they suggested, was related to an ageing process Breyfogle,[2] on the other hand, concluded from a comparable necropsy study that the association between gall-bladder disease and coronary artery disease was independent of age and sex Wolferth[3] wondered whether the two diseases shared a similar metabolic pathogenesis But there is a striking difference in the sex distribution of coronary artery disease, with male preponderance, which has not been found in disease of the gall-bladder

Whether gall-bladder disease aggravates angina pectoris is still uncertain, but there is now clear evidence that it influences arrhythmias McLemore and Levine[4] report 7 *cases of heart block and gall stones*, recent biliary symptoms had been present in all They concluded that the heart block was due to coronary artery disease or hypertension in 5, in 1 it was possibly congenital, and in the 7th it might have been due to diphtheria in childhood 5 had complete heart block with frequent Stokes Adams attacks, 1 had first degree heart block with sinus pauses and syncopal episodes and the 7th had an episode of transient complete heart-block accompanied by an upset of consciousness Preventive measures had failed adequately to relieve these attacks All these patients underwent cholecystectomy 4 were strikingly improved, with no subsequent attacks of loss of consciousness for six months or longer, preoperatively these 4 patients had experienced such attacks very frequently—up to four times a day The remaining patients were also improved, with definite diminution in the frequency of the attacks Anæsthesia was not thought to have contributed to their improvement Asystole during operation called for special measures in 3 of the patients but all withstood operation well McLemore and L reasonably conclude that in patients with Stokes Adams attacks, and especially where these have persisted despite treatment, disease of the gall bladder should be sought.

The physiological basis of cholecystectomy in heart block is not completely clear McLemore and Levine's clinical observation is supported by experiments on the frog,[5] and comparable but inconclusive observations have been made experimentally in man[6] Swallowing has been found to precipitate Stokes Adams attacks, Weiss and Ferris[7] recorded three cases in which Stokes Adams attacks were brought on in this way, and suggested that they were due to a vagal reflex In 1 of their patients a *traction diverticulum* of the œsophagus was present Distension of the diverticulum by a rubber balloon led to auriculoventricular dissociation and syncope Release of the distension was followed by a return to normal sinus rhythm and the disappearance of symptoms Atropine abolished the symptoms and the heart block Mackenzie[8] found in a patient with rheumatic carditis that either digitalis or swallowing delayed auriculoventricular conduction But it is still difficult to define the precise action of the vagus and the sympathetic nerves on the heart in the intact animal[9]

Another drug has been added to those that may be useful in the medical treatment of heart-block—namely, sodium lactate Bellet et al[10] have found *sodium lactate* of value in resuscitating the heart after cardiac arrest, in treating ventricular standstill in Stokes Adams attacks, and in otherwise *increasing* the ventricular rate in complete heart block The drug was given by intravenous injection or infusion

These two promising new methods of treating heart block will no doubt be widely tested Both may prove more commonly effective than the artificial pacemaker[11]

We regret to record the death of Dr C W BUCKLEY, who was senior physician to the Devonshire Hospital for Rheumatic Diseases, Buxton, and of Dr ROBERT FLEW, formerly physician to the Hospital for Sick Children, Great Ormond Street

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1 Walsh B J Bland E F, Taquini, A C White P D *Amer Heart J* 1941 21, 080
2 Breyfogle H S *J Amer med Ass* 1940, 114 1434
3 Wolferth C C *J Mt Sinai Hosp* 1942, 8, 1121
4 McLemore, G A jun, Levine S A *Amer J med Sci* 1955, 229 386
5 Buchbinder, W C *Proc Soc exp Biol N Y* 1930 27 540
6 Hedge G B Messor A L *Surg Gynec Obstet* 1948, 86 6
7 Weiss, S Ferris E B jun *Arch intern Med* 1934, 54 931
8 Mackenzie, J *Brit med J* 1906, ii 1107
9 Gregg, D E Coronary Circulation in Health and Disease London 1950
10 Bellet, S Wasserman, F, Brody, J I *Circulation* 195 11, 685
11 Zoll, P M., Linenthal A J Norman, L R *Ibid* 1954, 9 48

Special Articles

CALORIES AND CRICKET

J. G. FLETCHER
M.Sc. Manc., A.R.I.C.
MEMBER OF THE DIVISION OF HUMAN PHYSIOLOGY, NATIONAL INSTITUTE FOR MEDICAL RESEARCH, LONDON

DESPITE the international prestige attached to success in sport,[1] detailed physiological studies of the energy expenditure in team games are few. Although the calorie cost of baseball (Morehouse and Miller 1953), and even that of the eightsome reel (Passmore et al. 1952) are available no detailed study of the energy expenditure in cricket could be found in the literature.

In a recent study of the energy expenditure of young men engaged in their usual activities the problem of the calorie cost of games assumed some importance (Edholm, Fletcher, McCance and Widdowson 1955). Opportunity was taken to measure oxygen consumption during archery, tennis, squash, and batting and bowling at the nets, and to observe and time events in an inter college competitive cricket match of rather better than village-green standard.

TABLE I—ANALYSIS OF TIME SPENT BATTING AND FIELDING IN INTER-COLLEGE MATCH

Activity	Time spent (to nearest ½ min.)			
	Player 1		Player 2	
	Batting	Fielding	Batting	Fielding
ing				½
ading	1½	14½	8½	4½
ing bowling	3½		0	
rolling		4½		15½
alking	3	15½	2½	0
unning	1	½	1½	½
tal	9	35	18½	30

COLLEGE CRICKET

In the college game the mean scoring rate was 2·44 runs per over and the average time per over was 3 minutes 27 seconds. In table I an analysis is given of the way in which time was spent by two players during the match. The term 'facing the bowling' describes the time when the batsman is receiving the bowling and includes all stroke play. The time spent during fielding in picking up and throwing the ball was very short and is grouped with running.

The calorie cost of batting and bowling at the nets was measured with the subjects wearing a mask connected to a Kofranyi-Michaelis portable calorimeter. Balls were delivered at the same rate as during play and batsmen ran twice for each six balls bowled. The results for 4 subjects are given in table II.

The energy expenditure during play was calculated by analysing the time spent in the various component activities and multiplying these times by the experimentally determined energy expenditure for that activity. In calculating the calorie cost of bowling in the game the value for bowling at the nets was not used because at the nets there was more than one bowler and hence a slower individual bowling rate. In addition bowlers at the nets usually do more fielding than during actual matches. The results of such calculations are shown in table III. It appears that activity at the nets was comparable with tennis, while during play the calorie costs did not exceed that of walking.

TABLE II—ENERGY EXPENDED DURING NET PRACTICE

Player	Surface area (sq. m.)	Measured expenditure (kcal. per hr.)	
		Batting	Bowling
1	1·80	413·1	549·0
2	1·87	301·2	402·0
3	2·08	591·6	421·4
4	2·11	553·2	547·8
Mean expenditure (kcal. per sq. m. per hr.)		239·6	212·2

Although cricket is nothing like so energetic a game as football the calorie values given in table III appeared to be surprisingly low. On the other hand great variety is to be expected in the tempo of our national sport and in the skill of the participants and consequently in the energy expended. These results might very well not be representative of cricket in general, and it was thought worthwhile to calculate the energy expended in Test cricket to see whether similar or different results were obtained.

TABLE III—ENERGY EXPENDED DURING INTER-COLLEGE MATCH

Player	Surface area (sq. m.)	Computed expenditure (kcal. per hr.)		
		Batting	Bowling	Fielding
1	1·86	395·8	319·2	186·0
2	1·87	315·0	283·2	229·8
3	2·08	415·8	318·6	205·2
4	2·14	405·0	338·4	201·0
Mean expenditure (kcal. per sq. m. per hr.)		183·3	158·0	111·6

TEST CRICKET

During the 1953 Test series against Australia English summer weather accounted for 46 out of the 150 hours scheduled for play. For a further 4 hours the ball was out of play leaving 100 hours during which runs were scored at the rate of 2·38 per over. The mean time of an over was 3 minutes 17 seconds, the daily average ranged from 2 minutes 50 seconds to 3 minutes 40 seconds. Further details are given in table IV. The original data from which these figures have been calculated are given by Swanton (1953) and White (1954). The scoring rate per over and the average duration of an over are seen to be virtually identical for inter college and Test cricket.

TABLE IV—1953 TEST SERIES ENGLAND v. AUSTRALIA

Batting		Bowling		Fielding	
Total runs	4363	Total overs	1833	Total balls	11 030
From boundaries	1988	Overs per day	83	Boundary strokes	401
Extras	202	Overs per hour	18·3	Balls not scored from	8781
Other runs	2173			Other balls	1754
Mean rate per hr	43·6	Mean time per over	3 min. 17 sec	Balls taken in field	8099†
Running between wickets per hr	*6·6	Mean runs per over	2·38	Balls taken per fielder per hr	8·1
		Mean overs per bowler per day	13		

* Including running for byes and before boundaries signalled.
† Assuming ½ × 8781 balls taken by wicket keeper.

The figures given in table IV were used as the basis for calculating the calorie cost of fielding, bowling and batting although some assumptions were necessary—for example that all running was at a speed of 7½ m.p.h. and walking at 4 m.p.h.

Individual performances during fielding could not be obtained from the records. The number of balls from which runs were scored is given in table IV. The number taken by the wicket keeper is not recorded but probably varies between a half and a third. It is assumed that the remainder must have been taken by the 9 fielders and the bowler and this quantity was added to the number of scoring strokes, including boundaries, to give the total figure for balls taken in the field.

Fielding

Fortunately the hours of play in the five test matches totalled 100 hours, which simplifies some of the calculations The fielding rate for the individual is given by dividing the total number of balls taken (8099 assuming the wicket-keeper takes one third, or 6636 if he takes one half) by 100 (hours) and 10 (fielders), which gives a fielding rate between 6 6 and 8 1 balls per hour So a fielder will, on an average, take a ball once every seven to nine minutes, and since the infielders are most frequently involved, activity in the outfield must be slight

Many fielders spend long periods slowly moving about close to their set positions, while others may stand firm but exhibit body movements of interesting variety An allowance was made for the energy expenditure involved, by dividing the calculated standing time, into strolling and standing, in the same ratio given in table I—i e, standing strolling = 19 23 The component activities of fielding were classified as standing (40 4% of the time), strolling (48 9%), running to field (1%) (assuming an average run of 20 yards to field each ball, which is probably an overestimate), walking after fielding, walking between positions (assumed to be 22 yards apart), and walking to and from the pavilion (a total of 9 7%)

The probable overestimate of time spent running is balanced by the lack of any allowance for picking up and throwing the ball. These figures are summarised in table v, the computed mean expenditure for fielding is 50% greater than for standing alone and is equivalent to very slow walking

Bowling

A run of 10 yards for all bowlers and a return walk of the same distance for each ball bowled was assumed in calculating the calorie cost of bowling (table v) Activities were classified as running up to bowl, walking back, walking to and from fielding position and pavilion, and standing fielding during alternate overs The calorie costs of standing, walking, and running, as measured by Edholm et al (1955), were used The value for fielding is obtained from table v An average of 83 overs was bowled each day, and the individual bowler delivered one seventh of these

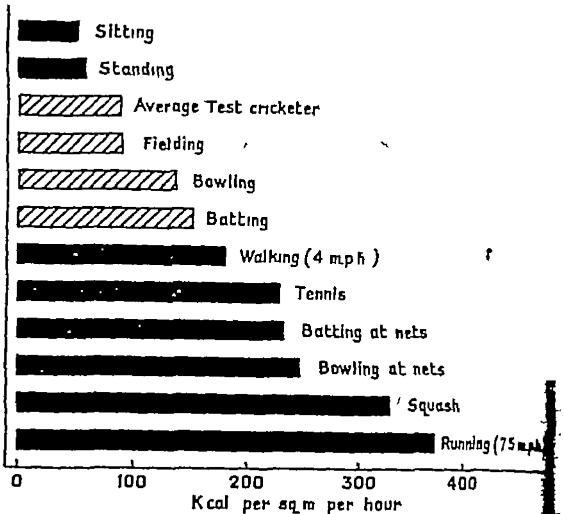
Batting

The figures given for batting in table IV show that there was running between the wickets for approximately half the runs scored The over all energy expenditure by batsmen (table v) was calculated from the measured costs for standing between overs, standing during batting of partner, batting, running, and walking to and from the pavilion The duration of each phase was computed, assuming the walking was at 4 m p h and the running was 22 yards per run at 7½ m p h The final calculation summarised in table v gives the average calorie cost as 155 2 kcal per sq m per hour

A separate analysis of the energy expenditure of the wicket keeper has not been made, as there is inadequate information available Umpiring and scoring have also been neglected

TEST PLAYERS

A final computation was made of the mean energy expenditure of that interesting but hypothetical individual, the average Test cricketer This player indulges himself in all four components of the game—he bowls 4 2 overs, taking approximately 14 minutes, he bats for 38½ minutes and scores 14 runs, he rests in the pavil for 116 minutes, and fields for the rest of the sched 6 hours of play per day His energy expenditure is at t rate of 86 4 kcal per sq m per hour—a value close that of fielding The accompanying figure shows h this expenditure compares with the computed expenditur of bowling, batting, and fielding in Test cricket, and w experimental values obtained from young men in o activities



Energy expenditure in young men (hatched = computed bl measured)

It remains to study briefly the probable energ expenditure of individual batsmen and bowlers of bo sides In the course of the 1953 series the maximu personal score in a day was 101 not out by Hassett in the second Test For the seven hours from the beginni of his innings it is estimated that the Australian capta expended energy at a rate 24% above the calculate mean, even assuming that he sat quietly while in th pavilion The increase was due to a high rate of scori and a high proportion of running between wickets. It was left to a Yorkshireman, Wardle, bowling ver economically in terms of energy and runs, to achieve the maximum number of overs in a day His analysi (36 overs, 14 maidens, 96 runs, 1 wicket) shows a hi proportion of maiden overs, while his energy expenditu as computed was approximately 9% lower than the me figure This is due to a short run up to bowl and relativel rapid overs According to the cricket correspondent of a London evening paper, Wardle took only 1 minute 48 seconds to deliver an eight ball over in Australia recently, as compared with times of 2 minutes 52 seconds, 4 minutes 17 seconds, and 4 minutes 25 seconds for Appleyard Statham, and Tyson respectively

TABLE V—ENERGY EXPENDED IN 1953 TEST SERIES

Activity	Batting		Bowling		Fielding	
	Time (hr)	Energy (kcal per sq m per hour)	Time (hr)	Energy (kcal per sq m per hour)	Time (hr)	Energy (kcal per sq m per hour)
Standing	47 8	67 6	22 6	57 6	40 4	57 6
Strolling *					48 9	88 5
Walking †	6 7	181 2	23 0	181 2	9 7	181 2
Running ‡	4 4	386 4	8 2	386 4	1 0	386 4
Batting	41 1	239 6				
Fielding			46 2	88 0		
Total	100 0		100 0		100 0	
Mean		155 2		127 0		88 0

* Equivalent to walking at 1–2 m p h
† Including between overs and to and from the pavilion
‡ Without additional allowance for throwing by fieldsmen

CONCLUSIONS

These calculations suggest that calorie expenditure sport is inversely proportional to the duration of effort. They indicate that in cricket better exercise is obtained at the nets than in the field The relatively small numbe of calories burnt by the average Test cricketer may hav some significant connection with the small bulk of th Ashes

REFERENCES

Edholm O G Fletcher J G McCance, R A Widdowson E
(1955) *Brit J Nutr* (in the press)
Morehouse, L E Miller A T (1953) Physiology of Exerc
St Louis
Passmore R, Thomson, J C, Warnock, G M (1952) *Brit J N*
6, 253
Swanton, E W (1953) The Test Matches of 1953 London
White C (1954) Cricket Annual 1954 London

CONN'S SYNDROME

(Primary Aldosteronism)

FROM AN AMERICAN CORRESPONDENT

At the recent meetings at Atlantic City of the American llege of Physicians, the American Society for Clinical vestigation, and the Association of American Physicians ch was heard of aldosterone (electrocortin) and of new disease entity involving the adrenal gland dis vered by Dr Jerome Conn of Ann Arbor Michigan is discovery may be as important to medicine as rvey Cushing's recognition of the syndrome which ars his name

In a presidential address last October to the Central ciety for Clinical Research Dr Conn described the case[1] a 34-year-old housewife who was admitted to hospital account of intermittent spasms weakness and alysis of muscles There were frequent attacks of eat muscular weakness and other attacks of typical tany involving the upper and sometimes the lower tremities She was well between attacks but the stolic blood pressure was known to have been 180– 0 mm Hg for four years For many years she had had uria and nocturia, and traces of protein were present the urine At the time of examination she was fit, ve for positive Chvostek and Trousseau signs. The ood pressure was 176/104 the size of the heart was rmal the reflexes were hyperactive and no oedema s present Biochemical studies revealed excessive ounts of aldosterone in the urine (equivalent to over 00 μg of deoxycortone acetate per day compared th a normal upper limit of 115 μg per day) There s severe hypokalæmia (serum potassium fluctuating tween 1 6 and 2 5 m eq per litre) The CO_2-combin g power was increased and the serum-sodium was ghtly increased to 151 A renal tubular defect in absorption of water was found and was thought to due to chronic hypokalæmia

Dr Conn pointed out the relative lack of important mptoms at extremely low levels of serum potassium e suggested that many cases of potassium losing phritis—such as that described by Evans and Milne[2]— ere really cases of primary aldosteronism At that me he prophesied that an aldosterone containing drenal tumour would be found when the patient was perated on, and he was right At the April meeting of e American College of Physicians he showed coloured hotographs of the large adrenal tumour which on say was found to contain tremendous amounts of dosterone compared with the aldosterone content of ormal adrenal glands

Last October Mader and Iseri[3] reported a case in hich the clinical picture was very *similar to that* scribed by Conn The patient was a 33 year-old woman ith tetany muscle pain weakness paresthesia hyper nsion and nervousness There was no history of omiting, diarrhœa or use of medicaments The serum iochemistry was disturbed: K 1 00, Na 143 Mg 1 12 a 3 05 CO_2 43 Cl 84 P 1 6 m eq per litre pH 7 5 rousseau's sign was positive, even after intravenous alcium gluconate but it gradually disappeared after rolonged treatment with potassium chloride Detailed orticoid-excretion studies revealed high absolute values for 17 hydroxycorticoid derivatives consistent with hyperfunctioning adrenal cortex Complete metabolic studies demonstrated (1) failure of correction of hypopotassæmia with a daily intake of 50 m eq K (2) pronounced negative Na balance and egress of Na out of cells during high K intake and balance (3) a slightly negative *magnesium balance on 12 m eq* Mg per day (4) loss of K in both urine and fæces; and (5) equilibrium of N balance Infusion of saline caused a distinct fall in serum Mg and plasma K without increasing urine Mg or K Profound electrocardiographic disturbance was only partly corrected by high intake of K Mader and Iseri felt that the syndrome was most likely due to adrenal cortical hyperfunction

Dr Iseri[4] said that they had recently operated on their patient—some three months after Dr Conn had had his patient operated on—and had found a large adrenal tumour which contained aldosterone Iseri now knows of two other patients with the same syndrome who had adrenal tumours and he has heard of a third patient in whom both adrenal glands were hypertrophied the glomerular layer being particularly large In this last case both adrenals were removed, and the patient recovered completely

The symptoms in these cases which are very similar to those previously described as "potassium losing nephritis," seem to indicate that aldosterone primarily affects potassium metabolism rather than sodium metabolism. But Dr John Leutscher does not believe that this is true The pathophysiology of the action of aldosterone was discussed at Atlantic City by Dr Laragh and Dr Stoerk and Dr Leutscher Laragh and Stoerk reported to the *American Society for Clinical Investigation* on the Mechanism of Secretion of the Sodium Retaining Hormone (Aldosterone) within the Body These investigators had previously demonstrated that *administration of potassium can produce a rise in serum* sodium that sodium-depleted subjects developed sustained hyperkalæmia after feeding relatively small amounts of potassium and that hypertrophy of the rat adrenal zona glomerulosa correlated with the level of serum potassium

Their present study was designed to determine the effects of changes in sodium and potassium intake and blood concentration on aldosterone secretion Synthetic diets were used in the study They found that restriction of dietary sodium in man even when combined with reduction in serum sodium produced slight to negligible aldosterone excretion unless potassium was provided in the diet When potassium was given in excess urinary aldosterone increased notably They took these findings to indicate that potassium is a powerful direct or indirect stimulus to aldosterone secretion Although dietary sodium restriction may exert its effect by modifying serum potassium or Na/K relationships within body water the data best support the hypothesis that change in serum potassium is a regulator—and possibly the primary regulator—of aldosterone activity

Dr Leutscher of San Francisco California, spoke at the meeting of the American College of Physicians, and reported that he had found high levels of aldosterone in cirrhosis nephrosis and congestive failure The increased urinary output of hormone seemed to correlate well with the presence of œdema and was inversely related to sodium excretion He also found that a high potassium intake lowered the urinary output of aldosterone

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1 J Lab clin Med 1955 45 3
2 Evans B M Milne M D *Brit med J* 1954 ii 1067
3 Mader I J Iseri L T *J Lab clin Med* 1954 44 895

4 Personal communication.

THE MIDWIFE IN THE MATERNITY SERVICE

In a memorandum on policy the Royal College of Midwives welcomes the provision, under the National Health Service Act 1946 for maternity medical services to be given by general practitioner *obstetricians and for* the attendance of consultant obstetricians should the need arise "but expresses its belief that the maternity service must continue to be based on the provision of an adequate number of well-educated well trained and experienced midwives The midwife today is trained to be the practitioner of normal midwifery, and as a member of the obstetric team she should be given a share in the planning and organisation of the service

Antenatal Care

The College thinks it of vital importance for the midwife to continue to exercise her clinical skill during the antenatal period

"Many doctors are now undertaking antenatal care in their own surgeries, but this does not absolve the domiciliary midwife from taking her full share of responsibility In hospital practice where the obstetricians attend every antenatal clinic, we consider it essential that there should also be antenatal sessions conducted by midwives

"The midwife has always been a teacher of individual mothers but today she is taking a much larger part in the antenatal teaching of groups of mothers Classes for the mothers in antenatal clinics should be organised by the midwife in coöperation with other members of the health team The midwife herself should give the teaching on the physiology of labour and the preparations for it, the use of inhalational analgesics, the preparations for the baby, and breast-feeding Provided she has had the appropriate experience, the midwife may, and often does, give instruction on relaxation and antenatal exercises to small groups of mothers

"In our opinion the assessment of the suitability of the home conditions for confinement should be made by the midwife in consultation, where necessary, with the patient's own doctor"

Care During Labour

Every mother, in the College's opinion, should be under the constant care of a midwife during the whole of her labour Although a doctor may be present for part of the time, the midwife should continue to take full responsibility for the majority of normal deliveries She can administer inhalational analgesics and, under the Dangerous Drugs Acts, she can give certain pain-relieving drugs It is thus within her power, and it is her duty, to give the mother adequate relief from pain during labour

Postnatal Care

During the postnatal period the mother and baby should if possible be looked after by the same midwifery team who cared for them throughout pregnancy and labour

"We deplore the practice in some hospitals of sending the mother and baby home, or to other premises, within a few days of confinement, since this makes it impossible to give them continuity of care

"The care of mothers and babies should remain the responsibility of midwives for at least 28 days It is the duty of the midwife to encourage the mother to attend for a post natal examination and to make the necessary appointment

"We are strongly of the opinion that premature babies should be nursed by midwives"

Administration

The College favours the formation of area midwifery committees with a composition similar to that of the Standing Maternity and Midwifery Advisory Committee of the Central Health Services Council In order to facilitate the smooth running of the maternity service, voluntary interchange of staff within the service should be encouraged Further the college holds that in both institutional and domiciliary practice the control of midwifery staffs should be by experienced members of their own profession

"All ad hoc maternity hospitals and maternity units of general hospitals, where there are 50 or more beds, should have their own midwifery matrons Where midwifery units are too small for the appointment of matrons, the superintendent midwife should have complete control of the unit and be held responsible for all technical and nursing care of the patients and the discipline and good management of the department She should be recognised as the appropriate person, in consultation with the matron, to engage pupil-midwives and other midwifery staff Arrangement of off-duty and holiday leave should also be her province

"Midwifery staff in these units should not be interchangeable with the nursing staff of the general hospital to which the unit may be attached

The superintendent midwife should have direct access to the appropriate hospital committees when matters affecting the midwifery department are under discussion and she should make the reports on her own department"

Every local health authority should, in the College's opinion, appoint a non-medical supervisor of midwives who should be a State certified midwife with the necessary experience This officer should be responsible to an administrative medical officer and should have access to the appropriate committee when matters with which she is concerned are under discussion

Recruitment of Midwives

There is today a grave shortage of midwives in some maternity hospitals and homes, particularly in those which are not training schools The need is not so much to attract more recruits into midwifery training as to retain the trained personnel in the practice of midwifery The College lays emphasis on the following points

(*a*) *Promotion*—There should be greater scope for the promotion of midwives within the profession More midwifery matrons should be appointed, so increasing the prospects of promotion and encouraging the midwife with administrative ability to remain in midwifery Newly qualified midwives should be given opportunities to take their fair share of responsibility in order to equip themselves for promotion to more senior posts "We believe that the midwife with additional qualifications should be considered for promotion on her merits as a midwife"

(*b*) *Auxiliary Staff*—The provision of adequate auxiliary staff, nursing and domestic, in maternity hospitals and homes would allow trained staff to devote more time to their specific duties for the mother and baby, and would thus make the conditions of practice more attractive to midwives.

(*c*) *Salaries and Conditions of Service*—It is most important that the heavy responsibility undertaken by the midwife and the irregular and long hours which she often has to work should be suitably recognised in her salary and conditions of service

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DOCTORS IN PARLIAMENT

In last week's General Election ten doctors were elected to Parliament Two of them are newcomers to the House of Commons—Dr D McI Johnson, Conservative member for Carlisle, and Mr J D Cronin, F R C S, Labour member for Loughborough

R F B Bennett, V R D, M.A, B M Oxfd, D.P M (C., Gosport and Fareham), was first elected in 1950

A D D Broughton, M A, M B Camb, D.P.H., D.P.M (Lab Batley and Morley), first entered Parliament by winning a by-election in 1949

J D Cronin, M B Lond, F.R C S (Lab, Loughborough) qualified from St Bartholomew's Hospital in 1939 He served in the R A.M C from 1942 to 1946 After holding appointments at the Royal Free Hospital and Great Ormond Street, he became orthopædic surgeon to the French Hospital in London He has been a member of the London County Council since 1952

Walter Elliot, P C, C H, M C, M B, D SC Glasg., LL.D F.R C P, F R S (C, Glasgow, Kelvingrove), first entered Parliament in 1918 *He held office as Minister of Health in 1938-40* He has represented his present constituency since 1950

Somerville Hastings, M S Lond, F R C S (Lab, Barking) a former chairman of the London County Council, was first elected in 1923

Charles Hill, P C, M A, M D Camb, LL.D, D P.H (L and C Luton), was secretary of the British Medical Association from 1944 until he entered Parliament in 1950

D McI Johnson, M A, M B Camb (C, Carlisle), qualified from St Bartholomew's Hospital in 1926 He is also a barrister at-law

Colonel Malcolm Stoddart Scott, O B E M.D Leeds (C, Ripon), was Conservative member for Pudsey and Otley from 1945 to 1950, since when he has represented Ripon

Barnet Stross, M B, M SC Leeds (Lab, Stoke on Trent Central), has been in Parliament since 1945

Edith Summerskill, P C, M.R C S (Lab, Warrington) represented Fulham West from 1938 until the recent dissolution

The photograph of Dr Bennett is by the *Evening News and Hampshire Telegraph*, Mr Cronin by Universal Pictorial Press and Agency Dr Hill by Elliot and Fry Dr Johnson by Lafayette Colonel Stoddart Scott by Navana Dr Stross by the *Daily Herald*, and the remainder by Press Portrait Bureau.

Dr CHARLES HILL

Colonel STODDART-SCOTT

Dr D McI JOHNSON

Mr WALTER ELLIOT

Mr SOMERVILLE HASTINGS

Dr R. F B BENNETT

Dr A. D D BROUGHTON

Dr BARNET STROSS

Dr EDITH SUMMERSKILL

Mr J D CRONIN

A NEW CHILD-HEALTH CENTRE

Ex Natal, ante natal, post natal is the comprehensive motto suggested by Prof Alan Moncrieff for the new Province of Natal Centre of the London University Institute of Child Health The centre was opened on May 26 by Mr G P Jooste, High Commissioner for the Union of South Africa, who said that the financial help given by the people of Natal, in founding it, was part of the "Salute to Britain Fund," which they collected as a gesture of sympathy for our war-time troubles

PILGRIM'S PROGRESS

How the fund came to be used in this way is a stirring story In 1939 the medical committee of the Hospital for Sick Children, Great Ormond Street, were already debating how the hospital might best collaborate with the preventive health services, and at the same time a committee at the British Postgraduate Medical School were discussing a plan for preventive pædiatrics By 1943 (and considering how our attention was occupied at the time, this must be regarded as fairly rapid going) informal discussions had taken place with senior medical officers in the London County Council, and the phrases "model infant welfare centre" and "model school treatment centre" were heard In 1946 the University of London Institute of Child Health, with Professor Moncrieff as director, was founded, and though it was tucked into the hospital, and using cubicles for offices, it began at once to investigate how a model welfare centre might come into being The borough councils of Holborn and St Pancras allowed the institute to use their centres for the teaching of preventive work, but money for building was scanty, and building prospects scantier But in the summer of 1947 this star-crossed project suddenly found friends Mr Rupert Ellis, the Mayor of Durban, mentioned, in the course of a friendly visit to Professor Moncrieff, that he was sorry the advent of the National Health Service had prevented the people of Natal from helping Great Ormond Street Hospital "*I remember gripping my chair hard*," Professor Moncrieff said at the opening ceremony, "as I launched into a tactful explanation of how the money *could still be used—for our model welfare centre*" The sequel was a message from Mr Ellis to the South African Gift Committee, and on Dec 4 news came that the institute was to have £106,888—the balance then remaining of the Natal Gift

During the next eight years—years littered with planning committees, building committees, architects' conferences, and applications for building licences (finally issued in 1953)—the London County Council had time to consider their own part in the scheme, and undertook to pay 90% of the cost of maintenance and all the salaries of medical and nursing staff By the time building actually began the original gift had increased to £120,000 by interest, though unfortunately the rise in building costs had kept pace

MODEL INFANT-WELFARE CENTRE

The new building stands, on land provided by the university, at the corner of Guilford Street, overlooking another site benign to children—that of the old Foundling Hospital In the long run it will house both the Province of Natal Centre and the Institute of Child Health, but so far only the centre has moved in The spacious ground floor is planned for maternity and child welfare work, with plenty of rooms for clinics (antenatal in the south wing, postnatal in the north), a waiting room large enough to be used for demonstrations, lectures, and meetings, and a playroom for toddlers opening into what—when the builders relinquish it to the gardeners—should be a pleasant leafy garden with a fig-tree in the middle This playroom, like almost every other room, and all the corridors, in the building, is heated from steam-warmed aluminium panelling in the ceiling—the steam being cleverly borrowed from the heating plant of the hospital A reinforced glass panel, reaching to the floor, gives even the smallest child an outlook into the garden, and is guaranteed to stand up without splintering to thumps, kicks, and toy trains flung in anger The playroom, with perhaps one or two others near it, is to be used as a crêche on two half-days a week, and if this proves a popular arrangement it may be extended We all know the drawbacks of the full time day nursery anyhow from the children's point of view, but a couple of afternoons a week in the company of other children is sometimes just what the pædiatrician prescribes for a child, and it can also provide a welcome break for the mother Unfortunately such sporadic attendance is not usually acceptable to day-nurseries, and hence few mothers can arrange it for their children The Province of Natal centre may be starting a new and useful pattern The ground floor also houses a shop for welfare foods and a demonstration kitchen Just outside the entrance is a covered perambulator store, on which an eye can be kept from the inquiry desk, just inside

MODEL SCHOOL TREATMENT CENTRE

On the first floor are rooms for those activities of the school health service which Professor Moncrieff describes as "more conveniently carried out at a clinic than in the schools"—such things as dental and orthoptic rooms, a minor ailments clinic, and a room specially equipped for the testing of deaf children. The child guidance clinic which has been carried on at the John Street centre will also be transferred here to continue its work On the floor, too, is the health visitors' room (there will be three of them and their superintendent) and also their common room where they can lunch and brew tea In addition there are changing-rooms and lavatories for the children—boys at one end of the building, girls at the other following the usual L C C plan

THE INSTITUTE

This floor will also contain the reference library of the institute, which is to occupy the third floor The two large research laboratories are equipped with a new practical type of bench, not built to the wall but fitted against it, with cupboards underneath which can be moved along on skids to any convenient position The water pipes to the sinks, and the gas pipes, running along the wall behind the benches, are thus easily accessible to the engineers, and the layout of the laboratory can easily be altered by changing the position of the benches On the landing outside is a cold room for storage of specimens

All the windows in the building work on pivots at the mid-point of the two long sides they can be turned completely over for cleaning, and adjusted at any angle for ventilation The decorations are the only part of the new building which seem disappointing, being mainly a timid shade of green, but no doubt gay curtains, some of which have already appeared, will make a great difference

This is an important venture, a remarriage of therapy and prophylaxis—two partners who should have known better than to get divorced

CENTRAL HEALTH SERVICES COUNCIL

The thunder of the *latest annual report* by the Central Health Services Council[1] is rather distant, for accounts of the two main tasks completed during the year—investigations of general practice in the National Health Service,[2] and of the internal administration of hospitals[3]—were published some time ago

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[1] Report of the Central Health Services Council for the year ended Dec 31, 1954 H.M Stationery Office Pp 26.

[2] Report of the Committee on General Practice within the *National Health Service* H M Stationery Office, 1954 *See Lancet* 1954, ii, 32

[3] Report of the Committee on the Internal Administration of Hospitals H M Stationery Office, 1954 See *Lancet*, 1954, ii, 741, 747

Mental Nursing

During the year the council set up a working party to djudicate on a difference of opinion between the tanding Mental Health Advisory Committee and the tanding Nursing Advisory Committee over nurses for ental and mental-deficiency hospitals The working arty unanimously favoured the training and employment f nursing assistants.

hortage of Dentists

In 1946 the Teviot Committee reported that until bout 20 000 dentists were in active practice there would e no likelihood of securing entrants more quickly than ey were needed The Standing Dental Advisory ommittee saw no need to amend this appraisal It ound that of 15 000 dentists on the Register many ere no longer in practice, some were practising outside e United Kingdom and many admitted to the Register ith Colonial qualifications were studying for higher egrees. Of the remainder who were practising some % were aged over 55 The committee concluded that nless some action is taken there will be an acute hortage of dentists in the near future ' The Minister of ealth and the Secretary of State for Scotland have since t up an interdepartmental committee to ascertain the asons for the lack of candidates of suitable quality and indicate remedies.

GENERAL MEDICAL COUNCIL

SESSION MAY 24–27

The General Medical Council met on May 24 and 25 nd its session was followed by the sittings of the Medical isciplinary Committee

After a presidential address by Sir David Campbell ummarised in last week's issue) the council considered rovisional proposals for abandoning the certificate in ublic health and consequent rearrangement of the urriculum for the diploma

Dr R. M F Picken, moving adoption of the report of a pecial committee set up last year, said that written and ral evidence had been obtained from interested bodies and persons. In general, the opinion was that no substantial amendment was required in the subject-matter prescribed n the existing rules, but it appeared that the provision whereby every candidate for the D.P H had first to obtain he certificate was serving no useful purpose and was proving inconvenient for teaching bodies The rules were considered sufficiently elastic to enable any licensing body to make provision for part-time courses The ommittee had drawn up draft rules abolishing the ertificate and making consequential amendments Candidates should have a fairly wide experience of linical medicine before starting their studies for the diploma and the proposed new rules laid down that candidate should not be eligible to enter for the examination until two years after he had been fully registered Dr Picken explained that the net effect would be the same as with the existing rule but persons who did not have to do a period of National Service would not be given an advantage.

The council agreed to circulate the draft rules, with an xplanatory letter, to the licensing bodies and teaching institutions and provisionally approved the draft introduction subject to any necessary adjustment when the rules were submitted in due course for final approval

Dr H Guy Dain moved the adoption of the report of the Pharmacopœia Committee containing the report of the British Pharmacopœia Commission He pointed out that doctors would have eight years in which to get used to writing their prescriptions in the metric instead of the apothecaries system Sales of the *British Pharmacopœia 1953* to date totalled 33 728 The *Addendum 1955* would be published on Oct 3 and would take effect on March 1 1956

On the second day of its session the council met in camera to consider various matters including it is understood questions concerning the medical curriculum

Medical Disciplinary Committee

The Medical Disciplinary Committee ordered three erasures from the Register There were no applications for restoration following disciplinary erasure.

TESTIMONIALS

In the past when the committee has postponed judgment the doctor concerned has been told to furnish the names of professional colleagues and other persons of standing who would 'be willing to testify to their knowledge of your conduct during the interval.' The form used at the present session differed by the addition of the word confidentially" Whereas previously the testimonials have on occasion been read in open session with the doctor present, this practice is no longer adopted by the committee—a change that was commented on several times at the sitting

One counsel Mr J L E Rees at the conclusion of a case in which judgment had been postponed said that, although it was appropriate that the testimonials should be confidential there might be something in them which the committee would take against the doctor He suggested that an abstract of such adverse references should be supplied otherwise the defence would be at a disadvantage

Mr C P Harvey the legal assessor said that this would be possible The question was whether it would be politic He was sure the committee would consider the point

In two cases in which he appeared, Mr E B McLellan, counsel, offered to help the committee if there was any point in the testimonials on which he could assist. The Legal Assessor replied that the testimonials were given confidentially They would lose a great deal of their value if they were given by people who knew that they were afterwards to be the subject of comment and argument by other people

NO ERASURE

Herbert Albert Kenneth Rowland, registered as of The Vicarage Cleator Cumberland B.M Oxfd (1945) had had judgment against him postponed from July 1954 for obtaining payment in respect of prescriptions improperly and dishonestly claimed to have been dispensed by him He was not present; but Mr McLellan counsel instructed by Messrs. Le Brasseur and Oakley solicitors to the Medical Protection Society said that a year ago in order to rehabilitate himself he obtained a medical post in the Transvaal Mr McLellan submitted that the practice of asking for testimonials was applied most easily when the doctor remained in general practice or in hospital work in this country It was not so applicable when he went to another country Dr Rowland was in the difficulty that the only two doctors with whom he was in contact were doctors in a subordinate position to himself The President announced that the committee judged Dr Rowland to have been guilty of infamous conduct in a professional respect but after careful consideration of the testimony to his conduct and what had been said on his behalf they had decided not to erase his name from the Register

The Registrar was not directed to erase the name of *Moreen Catherine O Brien* registered as of Endfield Woodhouse Sheffield M.B Sheff (1950) who was found guilty of infamous conduct in a professional respect in forging medical certificates for National Insurance purposes which purported to relate to herself Judgment had been postponed for a year

FURTHER POSTPONEMENT

Judgment had been postponed for a year in the case of *William Frank Cruickshank* registered as of Westwood Brechin, M B Glasg (1933) who had been found to have been convicted of being drunk and disorderly and to have been guilty of failing to visit or treat patients neglecting over a considerable period his duties as a medical practitioner under the National Health Service and disregarding his personal responsibilities to patients. Dr Cruickshank attended but was not represented The President told him that the committee was not satisfied that the testimony as to his conduct would warrant them discharging the case at the present time A further postponement of a year was ordered, in his own interests

ERASURES

The Registrar was directed to erase from the Register the name of *Robert Taylor Noel Simpson*, registered as of Wakering House, Great Wakering, Essex, M.B Belf (1942) This is subject to appeal to the Privy Council within twenty eight days Mr McLellan, who appeared for Dr Simpson, said that his state of mind was such that retention of his name on the Register could not be recommended

Ebenezer Francis Thomas, registered as of Round House, High Street, Tullamore, Offaly, M.R C S (1951), was charged with infamous conduct in abusing his professional relationship with a married woman, and with committing adultery with her, of which he had been found guilty by decree of the Divorce Court He was found guilty of infamous conduct, and the Registrar was ordered to erase his name from the Register This is subject to appeal within twenty-eight days

FURTHER CONVICTION

In May, 1954, the committee decided to postpone judgment for a further period of a year in the case of *Patrick Aloysius Gallen*, registered as of 89, Grant Street, Glasgow, C 3, M B Glasg (1929) He had had convictions in 1940, 1946, and 1952 for driving while under the influence of drink and for driving without due care and attention Mr Widgery said that there had been a further conviction against the doctor for assault In view of testimony to Dr Gallen's conduct, the committee did not direct the Registrar to erase his name from the Register

ABUSE OF DRUGS

Thomas Leven, registered as of 2, Beech Avenue, Irvine, Ayrshire, L R C P.E (1945), had had judgment postponed for a year in May, 1953, after a conviction for obtaining morphine sulphate, contrary to the Dangerous Drugs Regulations Judgment was further postponed in May, 1954, and November, 1954, in the light of medical reports Dr Leven now attended and told the committee that it was more than fifteen months since he had received his last withdrawal dose In view of the testimony to his conduct, the committee did not erase Dr Leven's name

NAMES NOT ERASED

In view of favourable testimony, the Registrar was not directed to erase the name of *Graham George Robertson*, registered as of 22, North Ridge, Bedlington, Northumberland, M B Edin (1934), against whom judgment had been postponed for a year after conviction for driving a motor car while under the influence of drink and in a dangerous manner

James Ross, registered as of 151, Park Grove, Barnsley, Yorkshire, M B Edin (1943), had had judgment postponed for a year after conviction for a series of drug offences In view of the testimony to his conduct, the committee did not direct the Registrar to erase his name

The Registrar was not directed to erase the name of *Herbert Trevor Duke*, registered as of 7, Manchester Street, London, W 1, M B Lond (1952), who appeared before the committee

In view of favourable testimony as to his conduct, the name of *Robert John Gordon Williams*, registered as of Rockdale, Abersoch, Caernarvonshire, M.R C S (1941), was not erased Judgment had been postponed from July, 1954, after two convictions for driving a motor vehicle when under the influence of drink

FURTHER POSTPONEMENT

Ralph Martin Case, registered as of 71, Gillott Road, Edgbaston, Birmingham 16, M.R C S (1934), M B Birm (1934), appeared for postponed judgment He had been convicted of unlawfully procuring dangerous drugs The President announced that the committee had postponed judgment for a further year

Patrick Joseph Conlin, registered as of c/o Barclays Bank Ltd, Dudley, Worcs. M B N U.I (1920), had been convicted of driving a car whilst under the influence of drink The committee postponed judgment for a further year

NAME ERASED

Francis Carminow Doble, registered as of 42–43, Dean Street, London, W 1, M R C S (1906), was charged with having been convicted at the Central Criminal Court on Nov 11, 1954, of unlawfully using an instrument to procure a miscarriage, for which he was sentenced to twelve months' imprisonment The Registrar was directed to erase from the Register the name of Francis Carminow Doble He has twenty-eight days in which to appeal

SHOOTING CHARGE

Robert Philip Strang, registered as of 40, Harley Street, London, W 1, M.R C S (1940), M R C.P (1946), had been sentenced to eighteen months' imprisonment at the Central Criminal Court in November for shooting Edward [illegible] with intent to do him grievous bodily harm Judgment was postponed for two years

DRUG OFFENCE

James McKenzie, registered as of 255, Rochdale Road, Middleton, Manchester, M B Aberd (1944), admitted convictions in 1954 of unlawfully procuring amidone for himself and of unlawfully procuring a dangerous drug The committee postponed judgment for two years, requiring Dr McKenzie to give names of persons who would be prepared to testify confidentially as to his conduct in the meantime

BREACH OF THE PEACE

Robert Lindsay, registered as of 8, St Ninian Drive, Inverness, M B Glasg (1945), admitted convictions for committing a breach of the peace in 1951, 1952, and 1955, and one of being found drunk in 1954 The President announced that judgment was postponed for a year

MOTORING OFFENCES

William James, registered as of Richmond Villa, Llandyssul, Cardiganshire, M R C S (1942), was summoned on a charge of having been convicted at Carmarthen in 1953 and again in 1955 of being in charge of a motor vehicle when under the influence of drink The committee postponed judgment for a year

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Public Health

QUARANTINE MEASURES IN POLIOMYELITIS

A P Goffe
M B Lond, Dip Bact
SENIOR BACTERIOLOGIST

Edith M Parfitt
B Sc Lond
SCIENTIFIC ASSISTANT

VIRUS REFERENCE LABORATORY, CENTRAL PUBLIC HEALTH LABORATORY, COLINDALE, LONDON

There has been much discussion about the possible value of quarantine measures in the prevention of poliomyelitis Agerholm (1953) suggested that all persons with any degree of contact with a patient after the 4th day preceding the onset of symptoms should be strictly quarantined for 15 days The expert committee on poliomyelitis of the World Health Organisation (1954) recommends that "Children with familial or intimate exposure should be confined to their homes for 21 days Adults need not be confined, they should refrain from association with children other than their own and should avoid intimate contact with adults"

Apart from the question of the advisability of applying quarantine measures, the practicability of their application would depend on the distribution and spread of virus in the community The measures might need to be applied to all infected persons if a significant limiting effect were to be obtained in the community However, the view has been expressed that "infection moves through a relatively narrow stream of the population" (Bradley 1952), and it has been shown that virus can be isolated much more often from associates of cases than from non-contacts and with the greatest regularity among household contacts (Brown et al 1954) On the other hand serological studies have shown the high frequency of subclinical infection The work of Melnick and Ledinko (1953) showed that at the time of a type 1 summer epidemic, the ratio of subclinical infections to clinical cases was as high as 175 to 1 in children aged less than 1 year and somewhat lower in older children This suggests that virus is much more widely disseminated than is apparent from the number of clinical cases

We describe here a small outbreak of poliomyelitis in a country district during January and February 1954 Part of the affected area had been under regular survey since 1951 Quarantine was applied under relatively favourable conditions Laboratory investigations were designed and applied to estimate the extent of infection with the virus in household contacts of cases and in sections of the community at large during and after the period of quarantine The findings indicate that the quarantine measures applied in this community did not prevent the spread of infection

Laboratory Methods

Examinations for virus were made by inoculating tissue-cultures with extracts of fæces or of sewage All the specimens were frozen as soon as possible and were transported and stored frozen till just before test.

Tissue-cultures —Epithelial-cell cultures were grown in plasma-lined roller tubes from explants of minced monkey kidney in a medium consisting of 95% synthetic medium 199 (Morgan et al 1950) and 5% horse serum Cultures were ready for use after 8–10 days incubation at 37 C After the addition of either stool or sewage extracts cultures were re fed if necessary usually at 5-day intervals. The presence of poliomyelitis virus was suspected if cultures underwent characteristic cytopathic degeneration (Robbins et al 1952) and was confirmed by neutralisation in tissue-cultures or by complement fixation (Le Bouvier et al. 1954) with type-specific hyperimmune monkey sera Similar cultures and cultures of HeLa cells (Scherer et al 1953) were used for antibody tests; fresh medium was added just before inoculation and was not changed subsequently

Fæces —10% aqueous suspensions of each specimen were centrifuged and each supernatant fluid to which antibiotics had been added was inoculated into 2–4 cultures Some of the specimens yielding negative results were re-tested after ten times concentration of the extract by ultracentrifugation for an hour at 40 000 r p.m. in a Spinco centrifuge

Sewage.—To obtain samples, gauze swabs were left in the sewers for three days (MacCallum et al. 1952) at thirty points which had been selected in 1951 for a survey (MacCallum et al 1953) Fluid squeezed out of the swabs was pooled and concentrated from about 1 5 litres to a final volume of 6 ml. by precipitation with ammonium sulphate followed by ultracentrifugation (Melnick 1947) Samples taken at individual points were treated individually by ultracentrifugation alone (Melnick 1947) Each sample was inoculated into 10–20 cultures 0·1 ml being used per culture

Water —100 ml of each sample was centrifuged at 40 000 r.p.m. for an hour and the entire deposit was inoculated into ten cultures

Tests for antibody —Sera from the cases and contacts were subjected to a neutralisation test in which mixtures of blood or serum dilutions and a standard dose of virus (100 TCD_{50}) were inoculated into tissue-cultures. From the school children 0·1 or 0 2 ml of whole blood was collected by ear prick and immediately diluted with 0 6 ml of saline solution containing a trace of heparin After sedimentation of the blood-cells the supernatant fluid was tested for neutralisation of type-1 poliomyelitis virus by inoculation into suspensions of HeLa cells. This modification of the technique has been found sensitive to traces of antibody and was therefore valuable for tests on such small samples of blood

Description of Area

Topography

The terrain is farming country in East Suffolk The Town A, of about 7400 inhabitants is surrounded by a rural district which includes several parishes of 50–400 inhabitants The town which lies on a main road and railway has some industry and a market It is served with piped water and drainage On the sewage system thirty points established for the 1951 survey had been used for regular quarterly sampling Each point received drainage from 9–100 houses. In the present investigation an additional point was selected receiving drainage from a few of these points and from other parts of the town about 650 houses in all No houses where cases of poliomyelitis had occurred nor any of the town's schools drained into these points The sampling was estimated to have covered 1450 houses with 4430 inhabitants, more than half Town A's population

Village B, of 96 inhabitants, obtains its water from various places and has no piped sewage Most families from the village visit the town for shopping to see the doctor, &c Children aged more than 11 years attend secondary schools in the town and children aged less than 11 years attend a primary school in the neighbouring parish ; this school had 21 children under one teacher Teaching was usually conducted in one room, and midday meals were served in a second room Bucket closets were provided outside the buildings but hands could be washed only in a small cloakroom inside the school and supplied with water pumped from a well apparently directly under the school house The contents of the latrine buckets were used to manure a plot of land 150 yards from the school Drinking water was brought in sterilised containers to the school from the town

History of Poliomyelitis in the Area

Records over the past thirty years showed that single paralytic cases had been notified from Town A in each of the years 1925 1948 and 1951 The rural district embracing Villages B and C had a less fortunate record for its total population of 19 280 In 1937 there was one case in 1947 four cases, 1949 five, 1950 three 1951 one and in 1952 four cases all paralytic

We had been interested in this area since 1951 Virus was isolated from the case in the town in 1951 and found to belong to type 2 (Goffe 1953) Sewage had been examined at intervals of three months since the spring of 1951 In 1951 sewage sampled 10 days after the onset of the case was shown by monkey inoculation to contain poliomyelitis virus, but this was not typed Virus was not isolated again until July and November 1953 when on both occasions a type 2 poliomyelitis virus was found

Present Outbreak

The order of events in 1954 was as follows

Jan 8 case 1 aged 3 years, from Town A, admitted to hospital with paralytic poliomyelitis.

Jan 11 case 2 aged 33 from Village B admitted to hospital with paralytic poliomyelitis.

Jan 12 case 3 aged 11 years from Village B admitted to hospital with paralytic poliomyelitis

Jan 13 case 4 aged 16 from Town A, admitted to hospital with non paralytic poliomyelitis. Conference to decide on quarantine measures.

Jan 14 quarantine imposed on families of cases 1–4 Collection of specimens started 8/17 household contacts found to be virus carriers

Jan 19–21 Virus found in sewage of parts of Town A, away from households of cases, and in sewage of household of case 4

Feb 4 21st day of quarantine 6/17 household contacts still virus carriers.

Feb 12 onset of paralytic poliomyelitis in case 5 aged 20 in Village C

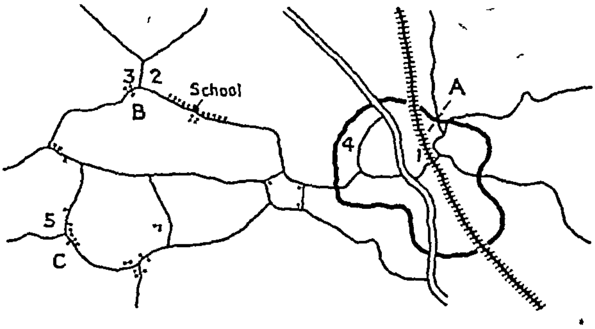
March 2 5/17 household contacts still virus carriers 1/18 school children of Village B found to be a virus carrier

March 8 quarantine lifted (54th day)

March 16–18 virus found in sewage of parts of Town A, away from households of cases

April 7 1/17 household contacts still a virus carrier (84th day)

It will be seen that during the second week of January 1954 four patients with poliomyelitis were admitted to



Sketch map showing location of cases 1–5 and village school and relation of town to surrounding villages

hospital, two from Town A and two from Village B Three of these cases were paralytic and one non paralytic, none of the patients became dangerously ill, but case 1 had considerable residual disability affecting both legs In the middle of February another case came to light in Village C, a woman complaining of weakness in the arms only Cases 1 and 4 came from different areas of the town, and had no known contact with each other directly or indirectly, or with members of the village families (see figure) Cases 2 and 3 were close neighbours in a group of council houses, obtaining a common water-supply from a deep bore-hole Case 3 attended a school in the town, his brother and sister went to the same village school as a daughter of case 2

On Jan 13 a conference was held between the medical practitioners of the town, the medical officer of health, the sanitary inspectors of the urban and rural districts, the director of the Ipswich Public Health Laboratory, and ourselves to decide on quarantine and other precautions to be taken, and on the scope of the investigation From the evening of the same day quarantine was applied to the families of these four patients Restrictions on the children were maintained until March 8, a total of 54 days In each of the four families children stayed away from school, had no contact with other children, and paid no visits to houses of other families or places of public congregation Adults avoided contact with others as much as possible, fathers continued at their work, and mothers were allowed to go shopping, but in some instances this was done for them by neighbours, who left the goods on the doorstep The only visits permitted to each house during the 54 days' quarantine were the periodic calls of the family doctor and the sanitary inspector in connection with the investigation

Samples of fæces were collected weekly for seven weeks and later from those still found to be excreting virus at the end of this period Blood samples were taken from the family of case 4 at the beginning, and from all the families at the end of the period A sample of tap water was collected from the house of case 1 on Jan 13, and a sample from the deep bore hole in Village B on Jan 14 Sewage from parts of Town A was collected, as described above, on four occasions Jan 15, Feb 16, March 16, and May 11 In addition sewage draining from the house of case 4 was sampled separately on each of these occasions Five days before three quarantined contacts returned to the village school samples of fæces and blood were collected from them and from all the other school-children and the teacher, three weeks later a second series of specimens was collected

Laboratory Findings

Examination of cases—Type 1 poliomyelitis virus was isolated from one or more specimens of fæces from four out of five cases (cases 1, 3, 4, and 5) Case 2, from whom virus was not isolated, was a typical case of mild paralytic poliomyelitis in a woman aged 33 Six specimens of fæces all yielded negative results However, she had type-1 neutralising antibody in her serum, and two of the four other members of her family were carrying the virus We conclude that her attack was also due to type 1 poliomyelitis virus

Examination of contacts—Type 1 poliomyelitis virus was isolated from the first specimens collected from eight out of seventeen household contacts None of these had any illness during the period of observation nor admitted to any symptoms suggesting minor illness during the preceding four weeks Of those found negative at the first examination none subsequently became carriers In three of the four families half or more of the household contacts were carriers, but in the family of case 3 specimens from all four members were consistently negative, moreover, one child in this family had no type 1 neutralising antibody in his serum Evidence of intrafamilial spread of infection was therefore lacking in this family Of all contacts from the four families there were eight children aged 1–10 years of whom six were virus carriers and nine adults of whom only two were virus carriers

Duration of excretion of virus in symptom free carriers—One of the eight symptom free carriers, an adult, was found to be carrying virus on the first examination only; in the remaining seven excretion was more or less prolonged one child excreted virus for 14 days, one adult for 31 days, four children for 48 days, and one child, aged 15 months, for 84 days

Examination of sewage—Type 1 poliomyelitis virus was found in sewage coming from parts of the town other than the houses of the cases, in the sampling both of Jan 19–21 and of March 16–18 This indicates the presence in the town of infected persons outside the families of cases, both at the beginning of the quarantine period and after it was over Virus was not found in the February and May samplings Type 1 poliomyelitis virus was also isolated from the swabs left in the drain of the house of case 4 in January and February, at which times four out of six and five out of seven persons respectively in the household were excreting the virus

Examination of school-children in Village B—One of the eighteen children at the village school was excreting type 1 poliomyelitis virus on March 2 but not on March 23, and thirteen out of the eighteen had type 1 neutralising antibody in their blood on both occasions None of the three quarantined contacts was excreting virus at the time of his or her return to school

Examination of water—Virus was not isolated from the samples of piped water of Town A and water from the deep bore hole in Village B

Discussion

This outbreak was favourable for observing the effects of quarantine measures, since it occurred in the winter with a small and easily observable number of clinically apparent infections and only one type of poliomyelitis virus, type 1, was concerned

Quarantine was applied to the families of the first four cases for 54 days, starting on the 5th day after notification of the first case and 12 days after the onset of the minor illness The restrictive measures conformed in general to those recommended by the World Health Organisation (1954) and by the Ministry of Health (1954) but their application lasted more than twice as long

In assessing the effects of quarantine measures it is important to take into account the fact that 47% of the household contacts were excreting virus when quarantine was applied There is no way of knowing whether the paralytic or the subclinical infections occurred first; moreover the dating of the outbreak from the onset of diagnosed poliomyelitis ignores possible preceding subclinical infections elsewhere in the community That this was in fact the case is suggested by the finding of virus in sewage from other households in the community during the first week of quarantine although type 1 virus had not been found at the sampling two months before the outbreak started A week after the raising of quarantine restrictions virus was again found in the sewage away from the cases' households The other community group outside of the cases' households that was studied was the school in Village B where five days before quarantine ceased one child was carrying type 1 virus and thirteen out of eighteen had serological evidence of infection at some time in the past with this virus It seems probable that infection had been travelling silently round the school during the time of the quarantine restrictions. Further evidence of the wide distribution of the virus is given by the occurrence of the fifth case from Village C four weeks after quarantine was started Thus, in spite of the restrictions on the contacts of the known cases, evidence was obtained of infection in the community during this period

The findings in the household contacts of the cases are of interest The proportion demonstrated to be infected with poliomyelitis virus *in the fæces* 8/17 (47%), is closely similar to that (41%) which has been found during outbreaks in the United States studied mainly by Francis and his colleagues (Brown et al 1954). The infection rate was much higher in the children than in the adults and the duration of excretion was longer in the children Only one out of the four households did not show evidence of intrafamilial spread In each of the families to show contact infection the youngest child showed the longest duration of excretion The *infant with its high susceptibility to infection* its liability to prolonged virus carriage and its untrained bowel habits provides both a rich source of virus and a ready means of dissemination into the household environment

The duration of excretion of virus by household contacts of cases of poliomyelitis does not appear to have been measured previously There were eight symptom free virus carriers in this group seven were still excreting virus 14 days after the first examination, six after 21 days five after 48 days and one aged 15 months, after 84 days. These durations of observed excretions probably do not represent the total period of virus carriage which may well have started before observations were begun Quarantine seems to be of doubtful value in practice if at the end of three weeks, three-quarters of the infected members are to be returned to the community still carrying virus Even when the period of quarantine was more than *doubled as for this study*, more than half the carriers were still infective at its termination

We conclude that the findings in the household contacts suggest that quarantine could not be an effective preventive measure in poliomyelitis and that the community studies show that in this instance spread of infection took place despite them

Summary

During a small outbreak of poliomyelitis in a country district in the winter months quarantine was applied to the households contacts of the first four cases for seven and half weeks.

Evidence *from virological studies is presented* showing that community infection took place despite the quarantine measures and the virus was found in sewage draining houses in which no clinical cases of poliomyelitis had occurred.

Eight out of seventeen household contacts of clinical cases of poliomyelitis due to type 1 virus developed infection without symptoms. 21 days after virus was first found six out of eight after 48 days five out of eight and after 84 days one out of eight were still carrying virus

It *seems* clear that under the conditions observed which were peculiarly favourable to the imposition of quarantine measures, infection was widely disseminated in the community and must have been spread by other means than by the patients and their immediate contacts.

We are grateful to the family doctors the sanitary inspectors of urban and rural districts, and the *medical officer of health* in the area concerned, as well as to the director of the Ipswich Public Health Laboratory all of whose collaboration made this investigation possible and to the Eli Lilly Fund, out of which the Spinco centrifuge was purchased

REFERENCES

Agerholm M. (1953) *Lancet* ii, 487
Bradley W H (1953) *Int Poliomyelitis Conf* p 143
Brown G C, Rabson, A S Schieble J H (1954) *J Immunol.* 73 54
Goffe, A P (1953) *Proc R Soc. Med* 46, 1091
Le Bouvier G L, Laurence G D, Parditt E M, Jennens, M G Goffe A P (1954) *Lancet*, ii 531
MacCallum F O, Cockburn, W C Smithard E H R. Wright, S L (1952) *Int Poliomyelitis Conf* p 484
— Goffe, A P Beveridge J J Phipps, A H Macrae A D Cockburn, W C (1953) *Congr int Microbiol.* vol. ii, p 71
Melnick J L (1947) *Amer J Hyg* 45 240
— Ledinko N (1953) *Ibid* 58 207
Ministry of Health (1954) Poliomyelitis Medical Memorandum
Morgan J L, Morton H J Parker R C (1950) *Proc Soc exp Biol., N Y* 73 1
Robbins F C Weller T H. Enders J F (1952) *J Immunol* 69, 673
Scherer, W F Syverton J T Gey G O (1953) *J exp Med.* 97 695
World Health Organisation (1954) *Tech Rep Wld Hlth Org* no 81 p 21

Poliomyelitis Vaccination

It is expected that mass immunisation of children against poliomyelitis in the United States will begin again shortly [1] In a statement on May 24 Dr Leonard A Scheele United States Surgeon General, said that " vaccine produced by all manufacturers has been proven to be safe except possibly the lots of Cutter vaccine Later he said that he expected Federal clearance for some vaccine early this week. The six manufacturers licensed to produce the vaccine have agreed to the government's proposals about safety standards, with '*more sensitive and more frequent*" testing of the vaccine

On May 27 the number of confirmed post-vaccination cases of poliomyelitis was 111

Control of London's Health Services

At a meeting on May 25 London Executive Council unanimously resolved that to transfer control of personal health services operated by the county council back to the borough councils would not be in the best interests of the population and ' in fact would be highly undesirable.'

The *executive council* had been invited by the county council to consider a proposal that certain health services should be transferred or delegated to the Metropolitan borough councils. At its meeting the council had before it a report by the local medical committee which also was unanimously opposed to such a change

In its report the committee remarked that since 1948, when London County Council took *over personal services from the boroughs*, much administrational duplication had been done away with The increased nursing staff now responsible for the whole of the child population had been integrated ; and the service was being " run with the utmost efficiency ' If responsibility were to be restored to the borough councils, the extent of some of the services would depend *entirely on the local rate* and those living in the poorer boroughs where the rates *are* highest would obviously suffer most ' It had been suggested that responsibility for the home health service should be divided between the county council and the borough councils but we have in the past seen the chaotic position of delegated responsibility in the tuberculosis service The committee observed that though it was proposed that the borough councils should *exclusively control the services* transferred to them, liaison between the boroughs was *to be* arranged to the satisfaction of the county council and this proposal was unworkable

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[1] *New York Times* May 25 26 27 and 28 1955

In England Now

A Running Commentary by Peripatetic Correspondents

In our little town, local pride boasts of three claims to fame—its salubrious salts, its generous accommodation for the mentally afflicted, and its Derby. Up on the downs, the hygroscopic chemicals in the soil give the turf an invigorating springiness which seems to communicate itself to the race-goers, and for those with time for reflection there is always the magnificent view of the pinnacles of the great mental institutions. There is a theory, popularly held after a trying outpatient session, about the indifferent mental health enjoyed by a singularly large section of the local population. This claims that many ex-patients settle here and raise families, for even they are aware of the unique attributes of the district.

On Derby Day one receives the distinct impression that all three major industries combine to ensure its success. Red-hot tips issue forth like sparks from a furnace and many a credulous victim has cause for regret after the race. The afternoon's work necessarily ceases, and those with outpatient appointments are seized with a sudden, though temporary, zest for fresh air. Among inpatients, no-one is too ill to take an interest in the commentary, and preparations usually begin in the morning with a popular clamour for the famous salts, whose pharmacological effect is ideally calculated to relieve all concerned from distracting thoughts at an exciting moment later in the day.

This year proved no exception in that losses were many and winnings were few. An inevitable gloom descended on the wards, impoverished tendon reflexes and subnormal evening temperatures were common, and the prospect of a forthcoming election failed to lift the depression. The only optimism sprang from a few undesirable characters who presented themselves at the casualty door in the hope of a night's bath, board and lodging, and theirs was short-lived.

* * *

He was a welcome change from the succession of dreary souls with faces as long as their list of symptoms, and tempers as irritable as their colons, and my heart warmed to his cheery face and twinkling eye as he puffed in medical outpatients. My surgical colleagues had obviously felt the same way about him, for they hoped that we would relieve his bronchial spasm as successfully as they had his retention.

Having duly percussed and listened, I was about to prescribe an antispasmodic and an expectorant when it struck me that his G P might already be giving him something of the sort. To my question he replied that his doctor prescribed a medicine, three times a day; a small pill, twice a day; an inhalation, one a day; and a linctus for the night.

"And do they help you?" I asked, thwarted. "Oh, I don't ever take them," he replied. "But you won't write and tell him that will you? It might hurt his feelings. You see, he is a fine doctor, and I have great faith in him."

* * *

XYZ was a normal English village and I had settled down to a peaceful holiday locum, when, one sunny afternoon, the telephone rang.

"Hello. This is Dr B—Dr A is on holiday. Can I help you?"

"This is Miss C, Miss D, who keeps bees, has just had a nasty sting and seems to be having a general reaction this time. I have already given her 'Antistin' and I was wondering if I should give her calcium?"

Miss C and Miss D were unknown to me—I had not even been warned about them—and Miss C's pharmacological knowledge appalled me.

"Well, Miss C, I don't understand why you wish to give calcium?"

"She has a generalised pruritus, Dr."

The word "pruritus" tripping so easily off the tongue made me even more uneasy and so in retaliation I asked:

"But do you have a preparation of calcium that can be given parenterally? No. (Good lord she understands that!) Well, I doubt very much whether the chemist here will have any either. Why don't you bring her round to the surgery and I'll see what I can do?"

Before their arrival I consulted the available vade mecums and was a little more at ease when they appeared. Miss D was easily dealt with. She had a generalised urticaria. Her eyes were puffy and bleary and she was so obviously uncomfortable that I got down to giving her adrenaline subcutaneously. Miss C was the real problem. She was a slender middle-aged woman made mannish by closely cropped hair. Throughout, whilst thrusting her hands deep into the go to hell pockets of her jeans, she lectured me on the anti histamines—never one of my strong points. At last, finding the going rather heavy, I asked her where she had learnt so much about these drugs.

"Just after the war, I became the keeper of the anthropoid ape section of the Munchausen zoo and, for a time, we had an allergic ape." Then as a wistful afterthought: "They're very like humans, you know!"

* * *

The car gently came to a halt about midway between York and Tadcaster. The time was 1 A.M., the nearest all-night garage was in York. After some time I was joined by the driver of a heavy lorry who stopped to offer help as is the nature of his kind. His tank was nearly full of petrol, but the task of transference appeared to be insuperable. The problem clearly was one of syphonage, and, in a moment of inspiration, the means became clear. The attachment of the two rubber tubes of a stethoscope to opposite ends of one earpiece supplied a syphon of effective length. The transfer of two gallons of the precious fluid was quickly completed and my journey home resumed.

My stethoscope was described by the makers as a dual-purpose instrument, and this claim appears to be justified. Perhaps the story should be entitled The Effective Use of the Stethoscope in Modern Medical Practice.

* * *

Not "In England" and not all of it "Now". When I was a R.A.M.C. surgeon in Egypt in 1945 I had so persistent a pain in my left renal area that I had an X-ray done. This showed nothing abnormal. A few days later my wife wrote from Devonshire that there was a new X-ray machine in the practice where she worked as a radiographer and her colleagues had used her abdomen as the subject of its first trial. The excellent films obtained showed a large stone in her left kidney. After the removal of the stone our health remained good until some months ago when I began to suffer from lassitude, loss of concentration, insomnia, and an ache in the suboccipital region. This led to a keener interest in the merits of vitamin B, barbiturates, and dextro-amphetamine sulphate, but with scant improvement. My wife consulted a gynæcologist two days ago and her ovarian cyst is to be removed in a fortnight.

Should I be blamed for failing to recognise my symptoms earlier?

* * *

In our family the teaching of citizenship or civics is pursued opportunistically rather than by plan, our main theoretical principle being to satisfy the child's thirst for knowledge as it is manifested. A golden opportunity presented itself on Election Day while we swallowed a hasty breakfast in order to get to the polling station.

Our eight year-old daughter courteously divided her attention about equally between her food and the unprepared talk we gave on the Constitution and the principles of democratic government by election. Our degree of success can be judged by her sole question:

"And what do you get if you guess right?"

* * *

Our hospital is taking its share in the road-safety crusade. Where the ambulance charioteers swing round the mortuary bend on the drive, we are to have a new notice—"DEAD SLOW."

* * *

Overheard outside the hospital after visiting hour

"I'm afraid he's in a bad way. He's got blood pressure and high blood pressure—so they can't do much for him. If they treat one it upsets the other."

Letters to the Editor

CIVIL SERVICE MEDICAL APPOINTMENTS

SIR,—My attention has been drawn to a letter signed Toad Beneath the Harrow in your issue of May 14 Your correspondent appears to be taking the Civil Service Commission to task for including in their advertisements for medical-officer posts in the Civil Service the phrase 'promotion prospects."

These posts were in the basic grade and there are at present 382 such posts Above these are 133 posts in the more senior grades, which are normally filled by promotion There is also provision for ' special merit' promotion in their existing posts for medical officers whose qualifications and experience are exceptional

The argument that promotion prospects disappear if senior posts are not standing vacant at the time of advertisement is to say the least, unusual It does not appear to be accepted by other employers

Civil Service Commission,
London, W 1

W H FISHER
Secretary and Commissioner

CANCER

SIR,—I read with interest and some amusement the ingenious argument against cancer education put forward by Dr Hazel Baker in your issue of May 21 Since I did not suggest the operation or perform it on myself I can only conclude that she advises all her patients to refuse an operation if there is any chance of cancer being present. Can pessimism concerning the disease go further?

The difficulty about her suggestion, that patients who do not understand their symptoms will report to their doctor at once is the fact that so often they give themselves the wrong explanation and in many types of cancer they delay six months or over a year as is proved by statistics. It is only by cancer education and talking freely about cancer that man (or woman) will become a less frightened and more reasonable animal

Yorkshire Council of the
British Empire Cancer Campaign.

MALCOLM DONALDSON
Director of Cancer Survey

SIR —May we as psychiatrists, comment upon Mr Donaldson s interesting article of May 7? It seems necessary to draw a distinction between true cancer phobia and cancer apprehension, terms which we think should not be used synonymously Educated and well informed persons may suffer from irrational fears and the true phobic patient will not be substantially influenced by reassurance or education his basic problem is an emotional one with deep unconscious roots

Whether education will bring the cancer-apprehensive patient to the doctor any earlier is an open question Surveys in this field have in fact been carried out in America and there is evidence to suggest that educated and cancer-conscious people may delay considerably in seeking help in the case of suspicious symptoms and signs In particular Bacon et al [1] found that of 40 women with breast carcinoma 28 were deemed to have shown neglect in consulting their doctors These women were not of inferior intellect and the delay was particularly remarkable in that all had been reached by cancer education and had thought of cancer at once

We have no ready means of advising the cancer experts on how to bring the cancer-apprehensive patient earlier to medical consultation We suspect however that delay in seeking help may not necessarily be evidence of ignorance or lack of information though admittedly much needless fear does indeed exist about cancer Delay in many cases may be indicative of the individual s emotional make up and the way in which he handles the difficulties that arise in his life The more mature and responsible the individual the more readily and realistically will he face the situation frightening though it may be

In short the problem is as much an emotional as an intellectual one

Southern General Hospital,
Glasgow

H I CLAPHAM
A BALFOUR SCLARE.

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[1] *Psychosom Med* 1952 14 453.

LOW-LACTOSE MILK FOR CONGENITAL GALACTOSÆMIA

SIR —The essential need in the treatment of congenital galactosæmia is the exclusion of lactose and galactose from the diet For infants and children with this disease, the most important dietary requirement is a low lactose milk preparation In the treatment of cases in Great Britain Bray et al [1] have given 'Nutramigen' but this is an American preparation and both dollars and a special import licence are required in order to obtain supplies Cox and Pugh [2] prepared their own synthetic food the casein of which contained 1% of lactose

We wish to report our success in treating a child with galactosæmia with a low lactose synthetic milk powder, and to recommend this food to others for the treatment of such children Messrs Trufood tell us that this special milk powder is not yet available through the ordinary trade channels, but that it can be supplied by them through hospitals

The patient a boy was first admitted to the Birmingham Children s Hospital at three months of age. He was marasmic, weight 10 lb 2 oz. (birth weight 10 lb 7 oz) and he had an enlarged liver jaundice and impaired liver function His urine contained 3 2 g of galactose per 100 ml and paper chromatography showed the presence of galactose only A galactose-tolerance test was carried out after a feed containing 5 g of galactose with the following results: blood galactose fasting 10 5 two hours 180 seven hours 31 5 mg per 100 ml. urine galactose total 1 3 g in a six hour collection following the feed.

Until he was seven months old the child was treated with nutramigen and made good progress on this food He was then given Trufood low lactose milk and his progress has been maintained satisfactorily

The principal nutriments in the low lactose synthetic milk powder were casein (washed) glucose maltose dextrin, and coconut oil The washed casein was first dissolved in a solution of mineral salts. After adding the fat and carbohydrate the reaction was adjusted to neutrality and the preparation completed by homogenisation, pasteurisation and spray-drying The approximate percentage composition of the final powder was protein 22 fat 22 carbohydrate 51 (dextrin 22 maltose 10 glucose 10) salts and water 5

In all four different batches of synthetic food have now been given to our patient The lactose content of the washed casein incorporated into two of these batches was 0·04% and 0·13% respectively giving values of 9 and 28 mg lactose per 100 g final milk powder

On the last occasion of testing (age fourteen months) after an 8 oz (227 ml) feed of the special Trufood milk containing 2 8 mg lactose blood galactose levels were: fasting nil forty five min 18 ninety min. nil mg per 100 ml ; urine-galactose fasting 11 one two and three hours nil four hours 11 mg per 100 ml These results indicate that the small content of lactose in this milk preparation did not cause any accumulation of galactose in the blood or lead to appreciable galactosuria

The lactose contents of the washed casein preparations were determined by the method of Harding and Downs [3] in protein free filtrates obtained by an application of the zinc hydroxide (Somogyi) procedure Blood and urine galactose concentrations were determined by the same method [3] as described by King [4] for blood, and applied to urine filtrates prepared by the lead carbonate purification procedure of Dittebrandt et al.[5]

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[1] Bray P T, Isaac R J Watkins A G *Arch. Dis Childh.* 1952 27 341

[2] Cox P J N Pugh R J P *Brit med J* 1954 ii 813

[3] Harding V J Downs C E *J biol Chem* 1933 101 487

[4] King E J Micro-analysis in Medical Biochemistry London 1951; p 23

[5] Dittebrandt M., Tenney M. West, E. S *J biol Chem* 1944 152 395.

The child is now seventeen months old, weighs 27 lb and continues to develop normally, both physically and mentally

We are indebted to Messrs Trufood for generously providing the powder for our patient

H B SALT
CONSTANCE A C ROSS
J W GERRARD

The Children's Hospital,
Birmingham

CARDIAC MASSAGE

SIR,—I have read with interest the article by Mr Neri and Mr Stevenson [1] The authors have brought out the advantages of their approach, which consists of an abdominal incision with subsequent splitting of the xiphoid process and blunt dissection of the sternal origin of the diaphragm through the foramina of Morgagni or "Larrey's spaces" The left pleura is subsequently opened and the whole hand is introduced into the chest

Although this may represent a "new approach" it differs little from the method used in 1902 by Porrier and even earlier by Mauclaire Wexler and Bromberg in 1951 described what they felt was a "new approach," in which the same anatomical dissection was made Subsequently Devine and Devine have introduced a somewhat similar technique Bost in the early 1920s described a similar procedure for exposing the heart In general, all of these approaches have similar disadvantages, which on occasion can be serious

After reviewing the records of over 1730 cases of cardiac arrest which have been sent to us, and which are included in our cardiac arrest registry, my associates Dr J William Hinton and Dr L Corsan Reid and I have concluded that the thoracic approach for cardiac "massage" is the method of choice for the following reasons

1 The transdiaphragmatic or other procedures initiated beneath the diaphragm, or other procedures initiated through the abdominal incision, do not display the heart directly as is possible with the thoracic approach By direct display the heart s activity can be assessed more accurately Ventricular fibrillation is not always recognisable by palpation, and therefore it would be more likely diagnosed by the direct approach

2 In about 15–20% of all cases ventricular fibrillation is present In such instances defibrillation is most reliably effected by the electrical defibrillator, and the thoracic exposure allows easy application of the electrodes

3 Drugs can be accurately injected in order to avoid the coronary vessels, and can be instilled into the heart-chamber for which they are intended

4 The pericardial sac may need to be opened and can be most easily approached through the thoracic route By such an approach the phrenic nerve is less likely to be severed We also believe that the proper closure of the pericardial sac is best accomplished through the thoracic approach

5 Manual massage through the thoracotomy incision results in more adequate cardiac output, and there is less chance of subsequent irreversible cerebral damage Clinical experience as well as repeated work on dogs has convinced us that proper massage should maintain a circulation only slightly below the normal level All experiments of which we are aware indicate that massage initiated through an abdominal incision does not bring about as great an output as does manual compression of the heart through the thoracic approach

6 It is often helpful to shunt additional blood to the brain and into the coronary circulation By the thoracic route the aortic can be pinched off with the fingers or with a rubber shod clamp just beyond the origin of the great vessels

The thoracic approach should be no less rapid than any other One need not be a thoracic surgeon to enter the intercostal space and expose the heart Artificial respiration must be maintained regardless of which route is used Neri and Stevenson describe their route as an avascular one, and it is quite possible that post resuscitative bleeding would be somewhat less, but the superior deep epigastric vessels pass through the space described In addition cardiac arrest often happens at times when aseptic technique cannot be followed, often one does not have time to put on gloves (Cardiac arrest is essentially a 3–4-minute emergency with few survivals after cerebral anoxia has persisted for more than 4 minutes) The approach described by Neri and Stevenson involves a risk of generalised peritonitis and also of empyema

It appears that in this country the thoracic approach is now used almost universally The survival rates are apparently greater with this route, many large medical centres have reported survival-rates of 60–80%

Department of Surgery,
University of Missouri,
Columbia, U S.A

HUGH E STEPHENSON, Jr.

DRUGS IN THE TREATMENT OF DEPRESSION

SIR,—In your annotation of May 21 you draw attention to the large doses of methylamphetamine which I have reported,[1] greater than those often suggested Sargant and Slater,[2] for instance, give the daily dose of amphetamine as up to 20 mg, adding that half the dose of methylamphetamine gives the same effect

The maximum daily oral dose which I have used has varied considerably, whether given as a single dose or divided into three doses before 1 P M The table below shows the maximum daily dose given to every patient I have treated at the late Dr Elizabeth Casson's Mount Pleasant Nursing Home The effect of each dose has been recorded by day and night observation

Daily dose (mg)	*No of patients*	*Daily dose (mg)*	*No of patients*
1 25–5	45	17 5–20	21
7 5–10	34	22 5–30	29
12 5–15	30	32 5–40	13

2 patients received a maximum daily dose of 1 25 mg., but 8 received 45 mg and 1 60 mg

Methylamphetamine should be administered with care and no increase of dose greater than 2 5 mg should be made, and then only after full knowledge has been obtained of the effect of the previous dose Psychological disturbances and psychoses have been produced by daily doses of 50 mg of amphetamine [3] so that any dosage of methylamphetamine above 30 mg daily should be approached with special caution

Bristol.

G DE M RUDOLF

HARDENED FATS AND LUNG CANCER

SIR,—Professor Yudkin (May 14) claims that margarine contains essential fatty acids, although there can only be a question of one, linoleic, and, in comparing margarine with butter containing linoleic as well as arachidonic acid, he must have used the higher figures for linoleic acid content in margarine and a low average for butter He omits to mention arachidonic acid content although this acid has a high biopotency and appears to be the principal essential fatty acid to be supplied by the food or synthesised in the body from linolenic or linoleic acid

In comparing margarine with butter, undamaged vegetable oils, and animal fats I could have drawn attention to the fact that certain hardened fats accentuate fat-deficiency symptoms but, as this seems to be due to an increased essential fatty acid requirement, I thought it unnecessary at this stage to go further into this question

Lung cancer is increasing rapidly, rural lung cancer incidence is much lower than urban, and female lung cancer in most cases is about 22% of the male These features are reflected in our knowledge of the essential fatty acids the average consumption of the acids is decreasing rural produce (butter eggs, bacon &c.) is rich in the acids there is a sex difference in the requirement of these acids and for female rats it is 25% of that for the males

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[1] Neri, L , Stevenson D L *Lancet*, 1954, ii, 1207

[1] *Practitioner*, 1955, 174 180
[2] Sargant W Slater E Introduction to Physical Methods to Psychiatry Edinburgh 1954 p 170
[3] Delay, J Pichat P Lemperière, T Sadoun R *Ann méd psychol* 1954, p 51

Copenhagen JOHAN F NYROP

SCHIZOPHRENIA OR GENETIC ENCEPHALOPATHY ?

SIR,—Adrian[1] and Murray[2] make clear that the brain can be grossly abnormal in the absence of microscopically demonstrable changes Penfield and Jasper[3] describe hallucinatory experiences many of which are typically "schizophrenic" except that they are episodic associated with epileptic foci in the temporal lobes, reproducible by stimulation and relieved by appropriate excisions Penfield and Jasper look upon the temporal lobes as the storehouses of rememberable experience The diagnosis of schizophrenia is not suggested by the total clinical picture: there are schizophrenic symptoms without psychosis.

The frontal lobes could hardly be responsible for less than is attributed to them by Penfield and Jasper—i e for planned initiative and the understanding of the future consequences of present action Jasper and Penfield state that stimulation of the frontal lobes does not produce the dramatic evidence of function revealed by stimulation of the temporal lobes but the fleeting distortion of planned initiative in a patient on an operating table would hardly be expected to do so although the same patient would soon run into trouble during the ordinary business of life if his planned initiative was distorted and his understanding of the future consequences of present action was seriously at fault Add some temporal hallucinations to such a patient and his perplexity and alarm are understandable Mental symptoms occur in the early stages of lesions in the "silent" areas,[4] and Miskolczy[5] suggested that the areas of the brain affected in schizophrenia are those which are typically human

The very considerable and convincing research on hypothalamic dysfunction in schizophrenia collected by Gellhorn[6,7] together with his own contributions, make it a reasonable proposition that in schizophrenia the lateral and posterior hypothalamus either is affected as part of the disease or is disordered by the disease (The lateral and posterior nuclei have developed throughout the mammalian series pari passu with the neocortex, both reaching the highest development in man[8]) Possibly both statements are true although I suggest that schizophrenia is more likely to produce autonomic changes than are autonomic changes to produce schizophrenia Anatomically[8] and physiologically[6,9] the functional integration between the cortex especially the frontal cortex and the diencephalon is so intimate that in the matter of nervous activity one is back with the hen and the egg At any rate add autonomic dysfunction to the frontal and temporal "paraesthesia" of the mind already suggested and the picture of schizophrenia is fairly complete

The evidence concerning heredity the early age at which schizophrenia develops, and the absence of any conclusive proof incriminating known pathogenic influences all suggest an inborn error producing ontogenetically inevitable pathology or pathology made manifest by factors not recognised at present to be pathogenic

The hypothesis is advanced that schizophrenia is a progressive disease process which throws regions of the brain into disorder and then out of action which spreads usually from the frontal poles backwards (although it may start in the temporal lobes or in the hypothalamus) and which spreads in tidal fashion with periodic recessions during any one of which the disease may become arrested It is further suggested that schizophrenia would be better known as phylogenetically and ontogenetically determined encephalopathy (the shortened term "genetic encephalopathy" would probably cause no difficulty despite other genetic encephalopathies)

If this hypothesis stands then:

(1) The disease must be unknown in animals and in very young children.

(2) Depending on the area first or mainly affected there would be indeterminate types

(3) Dysfunction in the hypothalamus would produce pituitary, suprarenal thyroid, and sex gland disturbances without actual disease in those structures.

(4) The early symptoms would be due to active disorder in brain cells, with dramatic symptomatology giving way more and more to loss of function and a form of mental defect. As a corollary "cures" of schizophrenia could result only in a level of human achievement which was less than that which might have been expected from early promise

(5) The electro-encephalogram would reveal atypical abnormalities, varying with the stage of the disease

(6) Patients with active disturbance could be helped by the removal or destruction in situ of parts disturbed

(7) However selective the toxin which imitates schizophrenia in its action, it would produce in addition effects on other parts of the brain, with more vivid and elementary hallucinations motor and sensory changes and disturbances of consciousness tending towards coma which are not observed in schizophrenia. Moreover such toxins would be most harmful to acute schizophrenics but cause less than normal disturbance in chronic schizophrenics.

St. Ann's Hospital
Canford Cliffs Dorset. D N PARFITT

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[1] Adrian E. D. *Brit med J* 1954 1 987

[2] Murray, E. G. D. *Lancet*, 1954 1 221

[3] Penfield W Jasper H Epilepsy and the Functional Anatomy of the Human Brain London, 1954

[4] Symonds C. P. *Proc R. Soc Med* 1931 24 100

[5] Miskolczy D In Scheffer and Miskolczy s Histopathologie des Neurons Leipzig 1938

[6] Gellhorn E. Autonomic Regulations. New York, 1943

[7] Gellhorn, E. Physiological Foundations of Neurology and Psychiatry Minneapolis 1953

[8] Le Gros Clark, W E Beattie J Riddoch G Dott N M The Hypothalamus London, 1938

[9] Daly J *Pr med* 1917 60 140

CHLORPROMAZINE

SIR,—Dr Vaughan and his colleagues (May 28) state that chlorpromazine is not a curative drug but this does not detract from its value as a "special" sedative and resocialising agent

Chlorpromazine is clearly more successful than dummy tablets but I feel it must also be controlled against drugs producing equivalent sedative effects before the word "special," as a description of its effect can be justified. Until this has been proved chlorpromazine should not be allowed to supplant the much less toxic cheaper sedatives in common use

It would be interesting to know if other methods of resocialisation had been used in the treated patients, such as nursing in groups with a total daily programme

I feel there is a danger of reverting to the massive sedation of chronic patients with even more toxic drugs and the recent advances in nursing techniques which depend upon an unsedated patient are in danger of being overlooked

Hill End Hospital
St. Albans G I TEWFIK

OCCLUDING FOLEY CATHETERS

SIR —Various forms of clips and clamps are used to occlude the inflating tube of Foley catheters Many of these devices are crude and heavy and cause permanent damage to the tube

A simple and effective method—for which no originality is claimed—makes use of a circular disc of thin tin plate or aluminium approximately 1¼ in. in diam tops of certain brands of intravenous litre flasks lise is bent to about a right-angle across its di tube is laid in the broad groove thus fo is then inflated and the disc is briskly the diameter in which the tube lies, and to this The whole forms a quarter-circle

The side tube is thereby firmly occlu sm is light in weight and will not

The cost is nothing I have never known the method to fail in securing and maintaining the inflation of the bulb Nor does it damage the delicate rubber tube

Royal United Hospital,
Bath
A T MATHESON

RESEARCH AND THE PATIENT

SIR,—Professor Witts (May 28) does Birmingham an injustice in implying that William Withering lived at Edgbaston Hall and established the use of digitalis "before the establishment of a hospital in Birmingham"

The hospital I have the honour to serve is the successor of the Birmingham Infirmary established under the Poor Law in 1740, and of high repute in Withering's time The General Hospital, Birmingham, was established in 1765, although not opened until 1779, Withering was one of the four original physicians

Withering settled in Birmingham in 1775 and began his ten years' research on the foxglove His earlier patients he saw at his consulting-rooms in Temple Row, and his later ones in the Square It is most unlikely that he ever saw patients (except in emergency) at Edgbaston Hall, and in any case he only moved into the hall a year after the publication of *An Account of the Foxglove* in 1785

Thus two hospitals had been established in Birmingham before Withering began his research, and he was on the staff of one of them while he was completing the research

Summerfield Hospital,
Birmingham, 18
ROBERT J HETHERINGTON

LUNG CANCER AND SMOKING

SIR,—I notice that in the investigations into the relation between tobacco smoking and cancer of the lung, research-workers generally expose animals to tobacco fumes or paint chemicals contained in tobacco on the skin There is also a lot of discussion about the compounds which may be vaporised and inhaled at the temperature of a lighted cigarette

Has anyone considered the possible importance of inhaled fragments of cigarette tobacco? The customary method of inhalation will on occasions carry a piece of tobacco down the respiratory tract Most smokers have at times experienced this, and small pieces would perhaps stay for long periods in contact with respiratory epithelium. Such events, if they occur by chance, would be more common in heavy smokers, and would not occur when an efficient filter is used. The insufflation of minute pieces of cigarette tobacco into the lungs of mice might be a profitable experiment

Virus Research Institute,
Entebbe, Uganda
CEDRIC MIMS

SIR,—The recent claim that there is a definite association between lung cancer and smoking in males raises the whole question of the validity of certain statistical techniques used in these inquiries I refer especially to the indiscriminate application of the χ^2 test and equal samples to statistical data

It is generally agreed that the χ^2 test is only applicable in a normal or nearly normal distribution with a well-defined tail at each end, yet in these investigations it has been used in what is a distribution of Poisson type and where a large sample is necessary before a tail will emerge to the right

The proportion of smokers among middle-aged men in the U S.A. is about 90%, and in England and Wales about 95%[1] In 1952 the number of male lung cancer deaths was 11,981, mainly among men of 30 and over, numbering 11,857,000 If an average expectation of life of 15 years be assumed for a lung cancer case we therefore obtain a prevalence (case-rate) of 1 5% for this disease There is reason to believe, however, that the lung cancer population in the male community is as low as 0 2%

Denoting by S and C the presence of the attributes smoking and lung cancer, and by s and c their absence respectively, in the male population, the following 2 × 2 table results, where p_1 and p_2 represent the probability of smoking and lung cancer respectively

	C	c	
S	x		Np_1
s			
	Np_2		N

Np_1 and Np_2 are the average number of smokers and lung cancer cases expected in a representative sample N of males and x is the number of smokers with lung cancer (CS) occurring in the top left hand cell

Np_1 is much greater than Np_2 and x can range from 0 to Np_2 The expected value of x on the basis of non association between S and C is $Np_1\,p_2$ which is close to the maximum value of x possible, namely Np_2

Given x Np_1, Np_2 in the sample N the values in the remaining 3 cells are obtained by differencing

Denoting the probability of a value x occurring, assuming no association between S and C, by Px, the probability curve of the distribution over the whole possible range of x is obtained from the formula

$$Px = \frac{(Np_1)!\,(Np_2)!\,(Nq_1)!\,(Nq_2)!}{(N)!\,(x)!\,(Np_1-x)!\,(Np_2-x)!\,(Nq_2-Np_1+x)!}$$

As an example, taking N = 1000 p_1 = 90, p_2 = 015 we g Np_1 = 900, Np_2 = 15 The expected value of x is $Np_1\,p_2$ = 13 5

x	Px
0	0000
7	0000
8	0002
9	0018
10	0100
11	0421
12	1287
13	2692
14	3445
15	2035
	1 0000

It is seen that low values of x are very improbable and the range within which x occurs according to chance is $N\bar{p} \pm \sqrt{N\bar{p}\bar{q}} = 13\ 5 \pm 3\ 5$ or 10—1 within which the maximum value of x possible—i e, 15—lies The χ^2 test could not be applied here as no tail exists to the right. For a tail to emerge Np_2 would have to be greater than 810 or N greater than 53,300

In testing the significance of the association between two attributes in a universe their respective frequencies must be considered This is quite a different problem to that of testing for the significance between the frequencies of a given attribute in two different and independent communities As an example of the first problem we have the association between smoking and lung cancer and of the second, a comparison of the incidence of dysentery, say, in London and Manchester Equal sampling can only be used in the latter type of problem

The 2 × 2 table of Dr Doll and Professor Bradford Hill[2] is an artificial one and not a random sample of the male universe It is so distorted as to form a veritable strait jacket for x, the possible range being 1289-1357, only 5% of the lung-cancer cases The distribution is the normal type with a tail at each end As would be expected the χ^2 test gives high significance

Assuming, for example, that the lung-cancer frequency is 1 5% the probability of obtaining equal numbers of C and c is $\frac{(2714)!\,(0\ 985)^{1357}\,(0\ 015)^{1357}}{(1357)!\,(1357)!}$ which is so improbable as to be impossible ($\log P < -1570$) The test is thus meaningless and leads to a false conclusion

According to the samples, the proportion of smokers among males is 97 5% and among non lung cancer cases 95·5%

	C	c	
S	1350	1296	2646
s	7	61	68
	1357	1357	2714

The number of lung-cancer cases is Np_2 = 1357 and, assuming p_2 = 0 015, these would be expected from a male sample N=90,467 The expected number of lung cancer cases among this sample of males would be 90467 (0 015) (0 975) = 1323 The maximum value of CS cases possible, namely 1357, lies within the range $1323 \pm \sqrt{1323}$, or 1287 — 1359, and therefore well within the range of values due to chance selection. So that if all 1357 lung cancer cases were smokers the fact would not be significant

The following table gives the minimum values for samples necessary for a tail to emerge to the right of the probability curve

p_1	p_2	Np_2	N
0 950	0 015	3370	224,670
0 955	0 015	4190	279,300
0 975	0 015	13850	922,300
0 950	0 002	3420	1,710,000
0 955	0 002	4250	2,125,000
0 975	0 002	14040	7,020,000

It is seen that in order to be able to apply the χ^2 test for significance, *assuming the proportion of male smokers* to be 97 5% a sample of at least 14,000 lung-cancer cases would be needed If the proportion of smokers however is taken to be 95% the least sample required is 3400

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[1] *Lancet*, 1952 ii 668

[2] *Brit med J* 1952, ii, 1271

To sum up, because of the high frequency of smoking and low frequency of lung cancer among males a greater proportion of smokers in lung-cancer males than among other males is to be expected and larger samples are required than those taken in order to show whether this is statistically significant moreover, the technique of equal samples in such an investigation is inadmissible Incidentally, it is difficult to see how an attribute with a high frequency like smoking can be the cause of a low frequency attribute like lung cancer

Bromley Kent. C A. GOULD

ELECTROPHORESIS OF PLASMA-PROTEINS

SIR,—From Dr Owen's letter of April 23 I understand that he is able to separate two components of the β-globulin fraction of the human serum by using paper electrophoresis He does not mention the time factor and the electric potential necessary to split the β globulin into its two components. This gives me an occasion to quote Wiedermann's paper,[1] describing a method of separation which I have confirmed in many cases[2] If the electrophoresis is performed in a wet tank (with 5-volt-per-cm filter paper a 'Veronal' Na HCl buffer, pH = 8·6 I = 0·05) not for the usual 8–10 hours but for 16–20 hours the β globulin falls into two components If the separation is continued for 20–24 hours the γ globulin will also separate into two components. Using a more alkaline buffer (pH 9–9 6) the separation becomes faster

Laboratory of the
Pediatric Clinic no II
University of Budapest. M. MILTÉNYI.

POTASSIUM DEFICIENCY AND KWASHIORKOR

SIR,—Hansen and Brock[3] reported that potassium retention exceeded the theoretical potassium/nitrogen ratio of 1/3 in 6 children admitted with diarrhœa, œdema and hypo albuminæmia All these children had hypokalæmia and in 2 treatment with a mixture of sodium and potassium salts alone was accompanied by electrolyte shift and loss of œdema They were careful to point out that all the children had œdema and diarrhœa while only some of them presented the other signs usually associated with the term kwashiorkor They may well be right in suggesting that electrolyte imbalance is important in the pathogenesis of nutritional œdema of the type they describe I am sure they would not claim from their experience in 2 children that it is the only factor involved in all such cases.

Heller and Schnieden[4] have shown that normal serum potassium levels may be found in children with kwashiorkor in Uganda These children all had œdema hypoalbuminæmia, and changes in colour and texture of the hair and/or skin Diarrhœa is a common but by no means universal feature of kwashiorkor as seen in the Kampala area of Uganda (it is probably less common here than in South Africa) Heller and Schnieden mentioned that severe diarrhœa was not a feature of the cases they investigated While agreeing with them that hypokalæmia is not an intrinsic feature of kwashiorkor in this area I should like to point out that potassium deficiency (which may exist in the presence of a normal serum potassium level) may be an important complication in cases with severe diarrhœa It may arise during treatment of children who have a normal serum potassium level on admission

It has been stated[5] that the diagnosis of potassium deficiency should be based on the existence of conditions predisposing to potassium loss In kwashiorkor with diarrhœa such conditions certainly exist and may be aggravated by high protein feeding after admission to hospital. The clinical diagnosis of potassium deficiency is particularly difficult in kwashiorkor since anorexia, diarrhœa, weakness, and less commonly vomiting are also features of uncomplicated kwashiorkor

Recurrence of anorexia specially if associated with vomiting abdominal distension, and weakness in a child with past or present diarrhœa, should I think make one suspect potassium deficiency Before this was recognised 9 out of 13 children presenting this picture went progressively downhill and died It is significant that 6 who received intravenous saline and glucose all died

Since the introduction of subcutaneous potassium therapy only 6 out of 15 such children have died Of these 2 had other severe complications, and only very limited potassium therapy was given to the other 4 Unfortunately many of the earlier children had to be treated without the serum potassium being examined Later estimations of serum potassium were made by the method of King[6] with the following results

	No of children	*Serum-potassium (m.eq per litre)*	
		Mean	*Range*
Children without kwashiorkor or diarrhœa	6	4 7	4 0–6 1
Kwashiorkor:			
No diarrhœa on admission	3	5 7	5 4–6 4
Diarrhœa on admission	7	4·0	3 1–5·6
Kwashiorkor with clinical potassium deficiency	4	2·6	1 6–3 5
On recovery	2	5 8	5 7–5 9

* 2 of these children had normal serum potassium on admission

Electrocardiographic signs were also non specific and cardiograms were not always obtainable. In 9 children with suspected potassium deficiency long P–R intervals (more than 0·14 sec) were found in half and flat T waves in all. There was no œdema of the chest wall when these tracings were made In 5 cardiograms were repeated during recovery although improvement was not dramatic all the cardiograms became normal except for one P–R interval which, although shorter was still outside the normal limit. QT was measured by several methods. The results were so variable even in the same cardiogram that no significance could be attached to the measurement

With this supporting evidence, replacement therapy was more energetically pursued, and children admitted with a history of diarrhœa, or who got diarrhœa later, are now given prophylactic potassium chloride (1 0 g daily) by mouth Children with subclinical deficiencies probably receive sufficient potassium in their milk to overcome their deficit.

Absolute evidence of potassium deficiency can be obtained only by dramatic response to intravenous therapy or by the demonstration of excessive retention by balance technique as used by Hansen and Brock. In view of the dangers of potassium intoxication it was considered wiser to rely on gradual replacement in these cases. Although the therapeutic response was gradual and therefore not diagnostic, the contrast with the fate of earlier children presenting a similar picture and not receiving potassium was striking In 2 cases serial cardiograms and serum potassium levels showed parallel gradual improvement

My regret that these findings are too few and not specific enough for detailed publication is mitigated by the fact that I have had no further cases presenting with severe potassium deficiency.

I am indebted to Prof A. W Williams for his interest and help in interpreting the cardiograms and to Miss M Lyle for some of the potassium estimations.

Mulago Hospital,
Kampala, Uganda M. D THOMPSON

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[1] Wiedermann D *Schweiz. med Wschr* 1953 83 1108
[2] Miltényi, M. *Kísérletes Orvost* 1954 6 369
[3] Hansen J D L. Brock, J F *Lancet* 1954 ii 477
[4] Heller H. Schnieden, H *Ibid* March 19 1955 p 618
[5] MacPhee I W *Brit med J* 1953 ii 528
[6] King E J Microanalysis in Medical Biochemistry London, 1951

Medicine and the Law

Inspection of Surgery

THE London Executive Council dealt last week with the case of a doctor who refused to permit the inspection of his surgery Clause 7 (5) of the N H S Terms of Service requires that a doctor shall permit the inspection of his surgery by a duly authorised member or officer of the local executive council

In March, 1955, the chairman of the London Executive Council directed that the surgery of Dr X should be inspected, and the practitioner was asked to state convenient dates and times Dr X wrote stating that he occupied a small flat part of which was used as a consulting room and living room, he was not prepared to allow any intrusion into his private dwelling and, as he had only a small list of patients, the question of inadequate waiting room accommodation did not arise Dr X further stated that, if his surgery was detached from his private dwelling, he would have no objection to an inspection provided it were carried out by an official other than a doctor, but his search for larger premises had been unsuccessful

Dr X was asked to attend before the medical service committee, but he replied that he was still unwilling to allow an inspection of his surgery to be made and that he did not propose to attend the meeting

The council decided to make representations to the Minister of Health that the sum of 5 guineas be withheld from Dr X's remuneration Dr X has twenty eight days in which to appeal

Diary of the Week

JUNE 5 TO 11

Monday, 6th

GUY'S HOSPITAL MEDICAL SCHOOL, London Bridge, S E 1
5 P M Dr J M H Campbell Acyanotic Congenital Heart disease (Carbutt lecture)
INSTITUTE OF OBSTETRICS AND GYNÆCOLOGY
4 30 P M (Chelsea Hospital for Women Dovehouse Street, London S W 3) Mr William Hawksworth Utero vaginal Prolapse

Tuesday, 7th

WRIGHT-FLEMING INSTITUTE OF MICROBIOLOGY St Mary's Hospital Medical School, Paddington, W 2
5 P M Prof B Ephrussi (Paris) Synthesis of Cytochromes in Yeast
INSTITUTE OF DERMATOLOGY, St. John's Hospital, Lisle Street, W C 2
5 30 P M Dr H J Wallace Vulval Atrophy

Wednesday, 8th

INSTITUTE OF DERMATOLOGY
5 30 P.M Dr R W Riddell Moniliasis and Related Diseases

Thursday, 9th

UNIVERSITY OF OXFORD
8 30 P M (Nuffield Orthopædic Centre, Wingfield Morris Orthopædic Hospital, Oxford) Mr William Gissane Problems in the Treatment of Injuries
ROYAL COLLEGE OF SURGEONS OF ENGLAND, Lincoln's Inn Fields, W C 2
5 P.M Prof Milroy Paul (Colombo) Hæmorrhages from Head Injuries (Hunterian lecture)
POSTGRADUATE MEDICAL SCHOOL OF LONDON, Ducane Road W 12
4 P M Dr Felope de la Balze (Buenos Aires) Normal and Pathological Testes
ROYAL SOCIETY OF MEDICINE, 1, Wimpole Street, W 1
5 P.M *Ophthalmology* Mr M. J Gilkes Cataracts associated with Neurodermatitis
INSTITUTE OF DERMATOLOGY
5 30 P M Dr Henry Haber Benign Epithelial Tumours
UNIVERSITY OF ST ANDREWS, Medical School, Small's Wynd, Dundee
5 P.M. Prof H A Salvesen (Oslo) Relation of the Parathyroids to Bone Metabolism and Bone Disease

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Friday, 10th

POSTGRADUATE MEDICAL SCHOOL OF LONDON
4 P M Mr P McG Moffatt Use of the Ophthalmoscope in Medicine (First of two lectures)
UNIVERSITY COLLEGE Gower Street, W C 1
5 30 P M Prof Otto Krayer (Harvard) Pharmacology of Veratrum Alkaloids the Anti accelerator Cardiac Action of the Secondary Amines
INSTITUTE OF OBSTETRICS AND GYNÆCOLOGY
3 P.M (Hammersmith Hospital Ducane Road, W 12) Mr A N C Walker Obstetric Fistulæ

Notes and News

WORLD HEALTH ASSEMBLY

AT the World Health Assembly in Mexico City last week, it was decided to expand the World Health Organisation's anti poliomyelitis programme Previous plans have included the setting up of a network of poliomyelitis laboratories in recent months to study the different strains of virus identified in each participating country, as well as other viruses responsible for diseases similar to poliomyelitis These laboratories are also studying the epidemiology of the disease and are making surveys of the natural immunity in different populations Two further tasks will now be undertaken the preparation and distribution of standard laboratory reagents in order to facilitate the work of national poliomyelitis centres, and the training of virus specialists in new tissue culture techniques used in this work A resolution was adopted to establish a world wide fund to assist national programmes for the eradication of malaria The fund, which would be fed by voluntary contributions from government and private sources, would be administered by W.H O The new fund would be devoted to the provision of supplies, equipment, and services to those governments whose needs could not be met through W H O's regular and technical assistance budgets

APPROVED NAMES FOR DRUGS

THE British Pharmacopœia Commission has issued the following new supplementary list of approved names

Approved name	*Other names*
Chlorhexidine	Bis *p*-chlorophenyldiguanidohexane Hibitane
Diethylthiambutene*	3 Diethylamino 1 1-di 2 thienylbut-1 ene Themalon
Dimethylthiambutene*	3 Dimethylamino 1 1-di 2 thienyl but 1 ene
Ethylmethylthiambutene*	3 Ethylmethylamino 1 1 di 2 thienylbut 1 ene
Methyl Phenidate	Methyl 1 phenyl 2 piperidylacetate Ritalin is the hydrochloride
Phenindione†	2 Phenylindane 1 3 dione Phenylindanedione Dindevan
Polymyxin	Antimicrobial substances produced by *Bacillus polymyxa* (Specific substances are designated by a terminal letter thus, Polymyxin E)
Streptonicozid	A compound formed by interaction of a suitable streptomycin salt and isoniazid Streptohydrazid
Triprolidine	*trans* 1 2' Pyridyl 3 pyrrolidino-1 *p*-tolylprop 1-ene Actidil is the hydrochloride

* Not intended for use in human medicine, diethylthiambutene is of interest in veterinary medicine

† Replaces phenylindanedione as the approved name

N.H S ACCOUNTS

FEW doctors, at the form filling end, would suggest that the National Health Service's methods of book keeping are lax and inadequate But the Comptroller and Auditor General in his annual survey of the N.H S accounts 1953–54 for England and Wales [1] and Scotland [2] once more politely voices the professional's slightly pained surprise at the amateur's apparent indifference to accounting niceties Thus he relates with approval that the Ministry of Health has drawn the attention of hospital authorities to his plea for the "normal system of competitive tendering for supplies,' but adds with distress that some hospitals still have not adopted or fully adopted the system One group of teaching hospitals who have for five years been refusing to interfere with house committee policy, have indeed agreed to reconsider the possibility of centralised group purchasing, but firmly add that "they would not expect more centralisation to result in better control of expenditure '

Again some hospital authorities have not yet completed the financial arrangements for the provision of medical services to local authorities, which the Ministry recommended at the beginning of 1953 Nor do the local authorities appear to have been coöperative Some have resisted claims made by hospital authorities, and owing to "difficulties of apportionment" some £122,000 for the period up to March 31, 1952 is still outstanding in the accounts of the Welsh regional hospital board.

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[1] H M Stationery Office 1955 Pp 41 2*s*

[2] H.M Stationery Office 1955 Pp 26 1*s* 6*d*.

The Comptroller in both reports refers severely to losses by fraud. Cashiers who take no annual leave and keys that are kept on tops of cupboards are in his view inconsistent with "normal accounting prudence Disciplinary action and inventories of stores also seem to him to show certain weaknesses.

Among his polite admonishments he has included some interesting facts. At Dec 31 1953 of the 1728 full time and 4684 part time consultants in England and Wales 2175 (33 9%) were receiving distinction awards, but the Ministry did not know the total cost nor how many awards went to full time and how many to part time consultants. Scotland is better informed and on March 31 1954 when there were 401 full time and 395 part time consultants, 74 (18 5%) full time and 140 (37 7%) part-time consultants were receiving awards of which the total cost was £220 408

The Comptroller also gives figures showing that the expenditure on compensation to hospital patients has risen from £23,636 in 1949–50 to £159 047 in 1953–54 The number of cases has risen from 507 to 1100 He points out that judgments in 1951 and 1954 have extended the hospitals liability until it now covers the whole of their staff "whether permanent or temporary resident or visiting full time or part time."

IRRADIATED BUTTERFLIES

An increased incidence of abnormally marked butterflies was reported from Japan after the atomic explosion at Nagasaki So Mr E M Elmhurst F.R.C.S of Ipswich, has been dosing caterpillars and pupæ of the Large Cabbage White Butterfly (*Pieris brassicæ*) with 200–1000r of X rays with a view to finding out if irradiation affects the distribution of pigment. The effects observed in human beings subjected to X rays are contradictory some skins darken others become paler The black areas on the wings of *P brassicæ* are due to the same pigment as is found in man—melanin Mr Elmhirst's results so far have been rather puzzling some butterflies appear normally pigmented but emerge from the chrysalis minus some of their legs or with broken antennæ. The greatest change in pigmentation has been a butterfly with grey instead of black patches on the wings but presumably this butterfly belongs to the spring or early summer brood and normally all the "black patches in this brood are grey—it is only the late-summer brood that has really black patches.

Genetic changes are also being studied and Mr Elmhirst has reached the third generation of inbred irradiated butterflies. The difficulty however in getting them to breed in captivity has led him to free them after staining the outer parts of the upper and lower surfaces of both fore and hind wings bright red with mercurochrome Anybody seeing any such *P brassicæ* is requested not to kill the butterfly but to let Mr Elmhirst know at Trophy House Grimwade Street Ipswich Suffolk, so that he can try to find their progeny About 170 have been freed and more are to follow Most of the reports of sightings come from the country to the west of Ipswich especially the vicinity of Colchester and Braintree; but one insect was sighted at Shoeburyness, and others have been reported from nearer London. This is not surprising for *P brassicæ* is famous as a migrant and usually travels westwards.

University of London

The title of professor of morbid anatomy in the university has been conferred on Dr C V Harrison in respect of his post at the Postgraduate Medical School of London.

Dr Harrison who at present holds the appointment of reader in morbid anatomy at the school studied medicine at Cardiff and at University College, London In 1929 he took the B.SC and M.B. of the University of Wales and the University of London After holding a house-appointment at the Cardiff Royal Infirmary he became assistant lecturer in pathology at the Welsh National School of Medicine In 1938 he took the M.D Lond Later he became senior lecturer in pathology in the University of Liverpool. His published work includes papers on sympathectomy in arterial disease and hypertensive and ischæmic heart-disease

At a recent examination for the academic postgraduate diploma in psychological medicine the following were successful:

R W A C Barton R H Gosling L A Hersov

University of Sheffield

Dr Margaret Middleton has been appointed clinical teacher in child health and Mr N W Reece honorary demonstrator in surgery

University of Edinburgh

Dr J H F Brotherston has been appointed to the chair of public health and social medicine in succession to Prof F A E Crew F.R.S who retires on Sept. 30

Dr Brotherston graduated M.B. from the University of Edinburgh in 1940 After holding house-appointments in Edinburgh he served with the R.A.M.C from 1941 to 1946 He spent the next year at the London School of Hygiene and Tropical Medicine when he held a Rockefeller fellowship in public health In 1948 he was appointed joint lecturer in social and preventive medicine to the school and to Guy's Hospital Medical School In 1949 he was given leave of absence to work, with a Rockefeller fellowship at Johns Hopkins University School of Hygiene and Pittsburgh University Graduate School of Public Health He was also a consultant to the United States Public Health Service. In 1951 he became senior lecturer in public health at the London School of Hygiene and for a year he was also part time divisional medical officer in south west Hertfordshire Two years ago he was appointed to the readership in public health at the school In 1952 he published a monograph on the early public health movement in Scotland

Royal Australasian College of Physicians

The following having satisfied the board of censors in Australia have been admitted to membership

D T Church B D Cotton A W T Edwards D A Ferguson R A B Holland R G Lewis D C Maddison R S Packard R D Spooner Claire Weekes (New South Wales) Peter Ebeling K F Fairley W S C Hare K H McLean, B W Neal J S Penington (Victoria) T M Ferrier (Queensland)

The following having satisfied the board of censors in New Zealand have been admitted to membership

W M W Brookfield R H Culpan P W Dykes G F Hall R W Hornabrook J D McGregor, J R Presland, D H H Pullon, F T Shannon C M Stubbs J M Tweed M H Watson R D Wigley

Faculty of Ophthalmologists

The following have been elected officers for 1955–56

President, Dr John Marshall, vice presidents, Mr T Keith Lyle Mr J R Wheeler, hon treasurer Mr A McKie Reid hon secretary Mr E F King

Beit Fellowships for Medical Research

The following elections have been made to junior fellowships (£800 a year):

P C Caldwell M.A., D PHIL. Oxfd To investigate the mechanism of muscular contraction in crustacea at the Marine Biological Laboratory Plymouth

R H Côté B.A B.APP.SC, D.SC, Laval Quebec. To investigate the chemical constitution of human blood-group substances of the A B and O Lewis systems, at the Lister Institute of Preventive Medicine London

Miss E I B Dresel M.A PH D Camb To investigate the biosynthesis of porphyrin pigments at University College Hospital Medical School, London

J M Lowenstein B.SC Edin PH D Lond To investigate the biosynthesis of pyrimidines in mammals at the department of biochemistry University of Oxford

R Whittam, B.TECH.SC Manc. D PHIL. Sheff To investigate the metabolism of adenine nucleotides in relation to the active transport of inorganic ions at the Physiological Laboratory University of Cambridge.

Little Committee for the Study of the Infantile Cerebral Palsies

A century after the publication of Little's classical descriptions of cerebral palsy this committee has been formed to study the clinical problems of diagnosis prognosis, and management and the administrative problems of training medical and other personnel for work on cerebral palsy The members are

Dr W R F Collis (chairman) Mrs Eirene Collis Dr William Dunham Dr L T Hilliard, Sir Francis Walshe F.R.S., and Dr David Lawson (secretary) Dr Lawson's address is Queen Mary's Hospital for Children Carshalton Surrey

Commonwealth Bursaries

The latest awards under the Royal Society and Nuffield Foundation Commonwealth bursaries scheme include the following

To Dr A A Kinnear Institute for Pathology, University of Pretoria, to enable him to study endocrinological techniques at Birmingham

To Dr J H D Millar consulting neurologist, Royal Victoria Hospital Belfast to enable him to study electrocorticography at the Montreal Neurological Institute

This is the third group of awards under the scheme instituted in 1953 to provide facilities for increasing the efficiency of scientists of proven ability by enabling them to pursue research learn techniques, or follow other *forms of study* in natural science in countries other than their own in the Commonwealth where the physical or personal environment are peculiarly favourable

Deutsche medizinische Wochenschrift

Original articles in this journal are now followed by summaries in English and Spanish.

Society for the Study of Fertility

This society is to hold a conference in Birmingham on June 23 and 24 Further particulars may be had from Mr H H Fouracre Barns, 31, Weymouth Street, London, W 1

Middlesex Hospital Medical School

Prof Corneille Heymans (Ghent) will give a lecture on the History of the Development of our Knowledge of the Physiology of the Baroceptors and Chemoceptors, on Tuesday, June 7, at 4 30 P M , in the medical school

Pembury Hospital, Kent

Two stained glass windows were dedicated by Bishop J C Mann in Pembury Hospital Chapel on May 22 to the memory of F Carter Browne and E C Hughes, surgeons to the hospital, and also of Amelia Scott, a social worker

Cambridge Graduates' Medical Club

The annual general meeting and dinner this year will be held at Jesus College on Friday, June 24 Members of the club who have not received a notice, or who have not yet notified their intention to be present, should communicate with Dr T B Anderson, 1, Huntingdon Road, Cambridge

International Congress on Diabetes

The second congress of the International Diabetes Federation is to be held at Cambridge from July 4 to 8, under the presidency of Sir Lionel Whitby On July 4 Dr Elliott P Joslin will deliver the Banting lecture of the British Diabetic Association He has chosen as his subject Diabetes for the Diabetics Further information may be had from the office of the congress, 152, Harley Street, London, W 1

Symposium on Stammering

The Goldsmiths' College announce a public symposium on stammering to be given on Monday, June 20, by students of Mr H V Hemery's speech re-education classes for stammerers. Of the three assistant chairmen, two will be members of the medical profession The meeting will be in the small concert hall of the college, New Cross, London, S E 14, and will begin at 6 45 P M

Royal Society of Tropical Medicine and Hygiene

The society's annual meeting will be held at Manson House, 26, Portland Place, London, W 1, on Wednesday, June 15, at 7 30 P M , when Prof R M. Gordon will be inducted as the new president Afterwards, to mark the centenary of the birth of Sir David Bruce, Sir William MacArthur will give an address entitled an Account of Some of Sir David Bruce's Researches, Based on his own Manuscript Notes

Postgraduate Medical School of London and Hammersmith Hospital

The school's 20th anniversary and the hospital's jubilee are to be celebrated next week On Monday, June 6, the Queen is to visit the hospital Wednesday, June 8, will be an Open Day, from 2 30 to 5 30 P M , when there will be an exhibition illustrating the school's research work, and doctors will be able to see a programme of medical films in the lower lecture theatre

Radioactive Materials in Biological Assay

This subject is to be discussed at a joint meeting of the biological and physical methods groups and the Scottish section of the Society for Analytical Chemistry with the Edinburgh and East of Scotland sections of the Royal Institute of Chemistry, the Society of Chemical Industry, and the Chemical Society on Monday and Tuesday, July 11 and 12, in the department of biochemistry, University New Buildings, Teviot Place, Edinburgh.

British Association of Urological Surgeons

This association is to hold its annual meeting from June 30 to July 2 at the Royal College of Surgeons of England, Lincoln's Inn Fields, London, W C 2, under the presidency of Mr Terence Millin The programme includes a discussion on Calcification and Calculus Formation in the Upper Urinary Tract, and at a joint session with the section of urology of the Royal Society of Medicine The subject is to be the Treatment of the Paraplegic Bladder

Medical Golfing Society

In the society's summer meeting at the Berkshire Golf Club, Ascot, on May 26, Dr J G H. McNabb won the *Lancet* cup (scratch medal 78) and the Henry Morris cup (2 up)

Inauguration of an Accident Service

From June 1 the Royal National Orthopædic Hospital, Brockley Hill, Stanmore (Grimsdyke 2900), is operating a twenty four hour accident service for the treatment of orthopædic injuries There are facilities for the reception of injured direct from the site of the accident Requests for admission or outpatient treatment should be made to the duty registrar

Investigation of Tonsillectomy

The South East Metropolitan Regional Hospital Board has approved plans for an inquiry into the value of tonsillectomy (*Times*, May 26) At Farnborough Hospital, Kent, and perhaps other hospitals in that area, 1000 children on the tonsils waiting-list will be chosen for the trial 500 will have their tonsils removed and 500 will not The health of the two groups in the succeeding year will then be compared.

Dr J Ferguson Smith has been elected an honorary member of the German Dermatological Society

Dr K. G Bergin British Overseas Airways Corporation's medical superintendent at London Airport has been elected a fellow of the Royal Aeronautical Society

Copies of the report on pre war diets, the subject of a note in our issue of May 21 have been sent to public libraries The Carnegie United Kingdom Trust has only a limited number of copies for further distribution

New British standards include a glossary of terms used in radiology (B.S 2597/1955, price 10*s*) and a standard for electrically heated blankets (B.S 2612/1955, price 3*s*) Copies are obtainable from the Sales Branch, British Standards Institution, 2, Park Street, London, W 1

Births, Marriages, and Deaths

DEATHS

BUCKLEY —On May 28 Charles William Buckley, M.D , F R.C.P., of Bentley Corner Ashbourne, and formerly of Buxton, in his 81st year

Appointments

BRATHERTON, D G , M B Camb , F F R., D M R T consultant radiotherapist as asst director of radiotherapeutic centre, and for East Anglian R.H B

DAVIDSON LAMB, WILLIAM M C M B Aberd D P.H deputy county M O H and deputy principal M O Gloucester

ELKINGTON, J ST C , M D Camb , F R.C P consultant neurologist, Royal National Throat, Nose and Ear Hospital London.

FEINMANN, E L M B Manc , M R C.P consultant chest physician, Gateshead Tuberculosis Administrative Area, Newcastle R.H.B.

HELM W H , M R C P consultant chest physician, Burnley and district hospitals, Manchester R.H.B

KUPER, S W A , M B Witw'srand D P H , D T M &.H , D C P whole time clinical pathologist and biochemist, Brompton Hospital, London, S W 3

MACKAY N R. M B Aberd , F R C.S E , D.M R T asst radiotherapist (S H M O) Royal Marsden Hospital, London, S W 3

MEARA, R H , M B Camb , M.R C.P asst physician Middlesex Hospital, London

NIKITIK CONSTANTIN, M D Lwow, D A consultant chest physician, South Shields H M C , Newcastle R H B

O'CONNELL, DANIEL, M B Dubl , D.M R first asst , radiotherapy department Charing Cross Hospital, London

THOMAS L P M B Wales F R C.S senior casualty officer, Cardiff Royal Infirmary, Cardiff

WALKER G B M.B Edin , D P H group medical superintendent Borders Hospitals board of management, South Eastern R H.B

WEAR A R , M.B Leeds, D O senior consultant ophthalmic surgeon special area committee Cumberland and North Westmorland and the Dumfries and Galloway board of management

London County Council

BARNES ROSALIND A M.B Lond , D P H , D OBST whole-time M O Public Health Department

HARVEY HAROLD, L R C P , D P H whole time M O , Public Health Department

SHORE ELIZABETH C L.R C P , D OBST whole time M.O. Public Health Department

Birmingham Regional Hospital Board

FRIEND J H , M.D Lond M R C P part time consultant physician Stoke on Trent group

LEVISON V B M.B. Lond , F F R , D.M R T whole time consultant radiotherapist, Coventry and Birmingham (Dudley Road) groups

RESPIRATORY INSUFFICIENCY*

A C DORNHORST
M.D Lond F R.C P
READER IN MEDICINE ST THOMAS'S HOSPITAL MEDICAL SCHOOL, LONDON

I HAVE chosen respiratory insufficiency as my subject because it is a common and important condition which is inadequately dealt with in most textbooks Moreover there has been in the last few years a good deal of work on disordered respiratory physiology It will be my purpose to show that this work although it has not ...sued in any dramatic therapeutic advance may be made to help in our everyday clinical tasks of recognising ...ssifying and assessing disorders

* * *

I should like to illustrate this by three very ordinary cases.

The first patient was a man of 45 who complained of ...ertional dyspnoea first noticed fifteen years previously and becoming steadily worse He had had no cough until ...r years previously, and had since had sputum only intermittently Physical examination and radiographic examination of the chest were unhelpful This history is of course suggestive of uncomplicated emphysema, but what clinched the diagnosis was observation of the patient during mild exercise When he walked briskly round the room nothing abnormal was at first noticed, but after a few minutes he was becoming uncomfortable and on halting was seen to be making respiratory efforts ...proportionate to the exercise and indeed his ventilation was probably greater than expected Moreover examination of his lips and tongue revealed a bluish tint which slowly disappeared as he recovered from the exercise

The second patient had a background disability similar to that of the first but he came under care in a ...y different way He was admitted as an emergency ...case and obviously very ill He was deeply cyanosed and his breathing was very distressed Numerous ...pitations could be heard over both lungs and the sputum was purulent The jugular pressure was raised but there was no oedema The patient responded rapidly to treatment with oxygen and antibiotics and returned to work as a hospital porter apparently none the worse

The third patient was a woman in her fifties who complained of swelling of her legs She had little cough and no sputum She was found to have considerable oedema, an enlarged liver and a raised jugular pressure—in fact she had heart failure She was strikingly cyanosed but not distressed and indeed she denied any difficulty in breathing The cyanosis could be mitigated by a voluntary increase in ventilation and was abolished by breathing oxygen which however made her stuporose

* * *

These three patients were all suffering from respiratory insufficiency the first in chronic form the second from an acute exacerbation with temporary cardiac overload of a chronic state and the third from a chronic form presenting as established cardiac failure These examples ...t so much as to make clear I hope the need for some ...y elaborate scheme of classification and to specify the patient's functional state we need I shall suggest at least four components or dimensions of classification The choice is suggested by the results of physiological measurements, but I shall first develop the ideas on a clinical basis.

The three patients described were all cyanosed though the first was so only on exercise This cyanosis was due to deficient oxygen saturation of the arterial blood and is characteristic of the disorder Indeed, we may take a decrease in arterial oxygen saturation on moderate exertion as the criterion of respiratory insufficiency

Why does the arterial saturation of such patients fall on exercise? In health this fall does not take place because ventilation increases more or less proportionately to the increase in oxygen consumption. The result is that about the same proportion of oxygen is removed from the inspired air and so there is little alteration in the composition of the alveolar air or in the gas tensions of the arterial blood If a normal subject voluntarily restrains his ventilation during exercise (and this can be managed), his arterial saturation will drop The patients we are considering behave as though their ventilation was not increasing during exercise by the normal amount But when we actually measure their ventilation we find as a rule that it is normal or somewhat raised It is clear then that they suffer from some failure to make proper use of the ventilation they achieve We may call this a *decrease in the ventilatory utilisation* which is our first functional component

We may then ask why the patients respiratory efforts are disproportionate to the exercise To some extent this may be due to excess ventilation but usually this is not itself sufficient and we conclude that the relation between mechanical effort and respiratory movement is changed so that the work cost of ventilation is increased We call this a decrease in mechanical efficiency which is our second component

Usually the patient's sense of subjective effort which probably reflects the output of the respiratory centre is in proportion to the mechanical respiratory work he is performing But sometimes this is not so For example in poliomyelitis with respiratory involvement the patient may feel very dyspnoeic—that is he is conscious of great respiratory effort, whereas the work achieved is small. We must therefore be prepared to take into account a reduction in the mechanical result of respiratory central activity a decrease in neuromuscular efficiency our third component

Finally we observe that some patients become very dyspnoeic on exercise when only slightly cyanosed while others are undistressed although grossly cyanosed at rest. Of course we should take into account also the arterial CO_2 tension and pH but when we do so we are still driven to the conclusion that there is considerable variation between patients in the response of the respiratory centre to chemical stimuli We can say that some patients have a decrease in the central sensitivity—our fourth component

Each of these components represents the relation characteristic of the patient at that time between two physiological variables which can be measured or assessed When the variables and the connecting component functions are arranged in order they form a closed loop Thus for a given metabolic rate, the ventilatory utilisation defines the relation between the *ventilation* and the blood gases determining the *chemical stimulus* The *chemical stimulus* will produce a respiratory central output or *drive* depending on the central sensitivity The *drive* will produce mechanical *work* depending on neuromuscular function and finally the mechanical function will determine what the *work* will produce in *ventilation* And so the loop is closed

The effect of this arrangement is that a deterioration in a function is not followed by a proportional change in the dependent downstream variable but by a smaller change combined with an increase in the upstream variables For example if the mechanical function and the utilisation were both halved and the total respiratory functional efficiency thus reduced to about a quarter of normal we should expect a deviation of blood gases on exercise not of four times normal but only of about twice normal, entailing about twice the normal *drive* and *work* and a near-normal *ventilation* This is a typical example of homœostasis, or, as it is now fashionable to call it, feed back stabilisation The arrangement benefits the patient by keeping the blood gases within limits as deterioration occurs, but it makes recognition of early abnormality more difficult In the above hypothetical example the *ventilation* might be normal, high, or low, according to the relative importance of the defects of mechanical function and of utilisation This emphasises the necessity of studying the relations between the physiological variables rather than the variables in isolation.

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* Frederick W Price memorial lecture delivered at Queen's University Belfast on April 20 1955

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I now turn to the methods of estimating the variables and thus inferring changes in the components These estimations may be made with differing degrees of accuracy, but the most accurate is not necessarily the most informative method, as there will nearly always be a price to be paid in applicability, continuity of measurement, and so on For many purposes of physiological research the time spent on an estimation and the coöperation required of the subject are not important limitations —in clinical research it is often quite otherwise Moreover, we can profitably use quite crude non-instrumental methods of quick clinical assessment

Thus there is no difficulty in measuring ventilation in a normal subject, but dyspnœic patients are intolerant of the usual mouth-piece and nose clip, and frequent cough and sputum may make their use impracticable Often a good compromise in such patients is continuously to record trunk expansion, which can be done without trouble to the patient, and to calibrate by a short run against a spirometer Clinically, it is fairly easy by observing trunk expansion to recognise over-ventilation during a standard exercise, if normal subjects have been observed under the same conditions One must recognise and make allowances for the see saw movements of chest and abdomen that often occur on exertion in patients with mechanical difficulties

The respiratory work is rather easily estimated by measuring intra-œsophageal pressure by means of a fine œsophageal tube, the pressure swing during the respiratory cycle multiplied by the rate of breathing is a fair index of energy used in expanding the lungs Clinically, increased force may be inferred from use of accessory muscles, indrawing of intercostal spaces, see saw movement, and so on

The respiratory drive cannot be directly measured, but it is probable that the subjective respiratory effort closely reflects it One can estimate what proportion of the maximum drive obtains at a given time by comparing the actual work or ventilation with the maximum the patient can achieve

The arterial blood pH and gas tensions which determine the chemical stimulus may be accurately measured in a sample obtained by arterial puncture but the methods are time consuming, and it may not be easy to obtain the samples—for example, during exercise A very useful instrument for clinical research is the photo electric ear oximeter, which allows the arterial oxygen saturation to be followed continuously at no inconvenience to the patient The advantage of a continuous record during exercise, hyperventilation, and oxygen breathing far outweighs any difficulties of exact calibration For clinical routine we have to rely on the recognition of central cyanosis This is notoriously difficult, but with practice and attention to detail one can often observe the fall of saturation on exercise The inside of the lower lip is probably the best place to look, and in a doubtful case it is always worth observing the effect of oxygen breathing, which often makes it clear by contrast that a patient that one might have been prepared to accept as normal was in fact too blue

By using these simple clinical methods it is ofte possible to place patients within the dimensions classification I have outlined Thus the first patien described became blue on exertion in spite of adequat ventilation He therefore had a significant defect utilisation His respiratory efforts were *unduly great fo* his ventilation, so he had a mechanical defect H subjective efforts appeared proportionate to his respiratory work on the one hand and to his cyanosis on th other There was therefore no need to invoke an alteration in neuromuscular function or in centra sensitivity By contrast, the third patient showed, striking lack of respiratory urgency in spite of dee cyanosis, and we may safely conclude that her centra sensitivity was impaired

* * *

I shall now review briefly the causes of deterioration in the different components, and must start by admitting total ignorance of the reasons why some patients retu full central sensitivity while others suffer an early and often gross decline When full sensitivity is maintained the patient complains greatly of dyspnœa, but because of his respiratory efforts maintains reasonable blood ga tensions for many years These patients are often suspected of making rather a fuss, and even of having hysterical hyperpnœa Those with more adaptabl centres have at first an easier time of it, but chronic anox heart-failure will eventually develop, and their average survival is probably shorter than that of the first group

Neuromuscular inefficiency is not commonly important factor It may occur in nervous system diseas such as poliomyelitis, or in disorders of muscle such dermatomyositis It may also be produced by abnormality of the thoracic cage rendering muscu action ineffective for example, the kypho scolio thorax may so lack stability that intercostal contract leads to a twisting of the cage with little expansion, the maximum negative pressure the patient can deve is much reduced

It is rare to find a patient with respiratory insufficien who has not at least moderate mechanical impairme Sometimes, as in severe asthma, it may be the o abnormality There are two main processes by which mechanical efficiency may be impaired The less comm is a decrease in lung distensibility due to fibrous repl ment of elastic tissue Although some degree of l fibrosis is common, serious impairment of distensibi is rare, probably because the sponge like structure al expansion even when the substance is relatively inext sible Some of the stiffest lungs I have personally inv gated have followed heavy radiotherapy One need ha add that the radiographic appearance is no guide to disability from this cause The lungs also become distensible during the pulmonary congestion of he failure The mechanism is obscure, and its discuss outside the scope of this lecture

The commoner mechanical disability is an incr resistance to the flow of air This may of course be i large airways as in tracheal compression, but usually is due to changes in the small bronchi and bronchi I would here like to interject a protest against common habit of assuming that any wheezy patie suffering from “bronchospasm” Of course it may so, but often the evidence suggests mucosal thicke or excessive exudate rather than excessive contractio bronchiolar muscle

In emphysema an airway resistance rising rapidly expiration is characteristic This is probably due to collapse of bronchioles in the absence of the normal pull from surrounding lung, and is the main cau decreased vital capacity in the common form emphysema

Limitation of vital capacity from whatever entails supernormal respiratory rates as very rases which in turn entails some wasted effort in a dead-space ventilation The importance of this ands on the airway resistance if normal, as for aple in ankylosing spondylitis, limitation of vital city causes little disability if high, as it often is mphysema, it contributes considerably to the total len.

here are two main causes for defective ventilatory ation the more apparent which is much the less mon, is a decrease in the area of alveolar membrane thickening or other impediment to diffusion A acteristic of this type of disorder is that it affects gen transport but not that of carbon dioxide This is use diffusion, being dependent on solubility, is some nty times faster for carbon dioxide and so this gas easily reach equilibrium between air and blood even n oxygen fails to do so Various diffuse chronic mmatory states—for example sarcoidosis and stosis—occasionally cause this type of defect

he commoner defect has a more subtle basis in local roportion of ventilation and perfusion One can see this can lead to inefficiency by considering a carica e of the situation in which all the blood went to one g and all the air to the other In emphysema, whether ted or associated with other disease, this type of tilation/perfusion mismatch is present in small regions oughout the lungs. It will be seen that this process airs transport of carbon dioxide as well as of oxygen ugh the latter is more affected because of its non ar dissociation curve

striking feature of the clinical course of patients h this disorder is the abrupt reversible deterioration respiratory function that accompanies a bronchiolar ction Of course some of this is due to increased way resistance, and as it is impossible to obtain mplete measurements from these very sick patients cannot say exactly how much Nevertheless, I am ly confident that infection reduces utilisation as well mechanical efficiency The practical implication is at the outlook of a patient with severe respiratory fficiency is better if his sputum is purulent for nsiderable improvement may be expected if as is usual sputum can be rendered mucoid by chemotherapy

* * *

This brings us finally to consider treatment where it st be admitted that the outlook is bleak if not entirely ren. Most can be done for increased airway resistance the sputum is purulent antibiotics are indicated; chospasm is best treated by an isoprenaline spray for persistent non-spasmodic wheezing (possibly due mucosal thickening) corticotrophin or cortisone should tried. Incidentally the method of direct estimation of way resistance indicated earlier has shown how difficult may be to assess the action of antispasmodics. In ticular, drugs with a striking general action such as ophylline given intravenously are often credited with ducing some benefit even though measurement shows change. On the other hand, I doubt whether chospasm in the strict sense, is ever completely enaline insensitive

s of central sensitivity poses an interesting thera tic problem Since the depression probably shortens patient's life one would like to attack it even though patient might not be very appreciative If an reased rate of ventilation can be maintained for several s it is reasonable to expect the centre to regain itivity as the carbon dioxide tension falls, in a way parable to the enhanced sensitivity attained at high itudes This has in fact been achieved by strenuous erventilation in a tank respirator; but this is a tour force a tank respirator being scarcely tolerable to a ient with much sputum and usually ineffective where re is much mechanical disability Another approach by the use of stimulant drugs My colleagues and I have made some trials with a nikethamide drip This is certainly effective in increasing ventilation and in arousing a patient with severe carbon-dioxide retention The difficulty is that when the patient is fully conscious he will not tolerate the drug in the high dosage required (250–500 mg per min) A personal trial at this dose level produced a most unpleasant burning and itching of the skin Another drug we have tried is salicylic acid which also increases the central response to carbon dioxide It may well be effective in some cases, but the respiratory action is difficult to dissociate from undesirable effects such as fluid retention

If one cannot be confident of restoring the sensitivity one can at least refrain from depressing it further with morphine which is indeed often rapidly fatal in these patients

In the episodes of acute insufficiency as in the second patient described earlier oxygen should be used It may be given by a tent or by a mask of the plastic nose bag type but the B L.B mask is unsatisfactory It is true that the removal of the anoxic drive decreases ventilation and so worsens the respiratory acidosis, and that this leads to drowsiness and even coma but if one is aware of it and uses common sense there is very little risk.

For chronic anoxic heart-failure therapeutic myxœdema produced by methylthiouracil has a place The patient is rendered more comfortable and may survive for several years The appearance of these deeply cyanosed myxœdematous patients is formidable and often someone is eventually moved by æsthetic considerations to interrupt treatment, with the usual sequel of a rapid return of severe failure

* * *

I hope I have made good my claim that physiological studies can help in the clinical management of respiratory insufficiency Sometimes the help is a direct estimation of some function More commonly it is by suggesting what to look for and reminding us of our errors that clinical technique is improved In this way the worker with special techniques learns new physical signs and becomes more adept at evaluating old This is an aspect of clinical research which is often undervalued

THE EFFECT OF HYDERGINE ON UTERINE ACTION

T N A JEFFCOATE
M D Lpool, F.R C.S.E F.R C O G
PROFESSOR OF OBSTETRICS AND GYNÆCOLOGY

J K WILSON
M.B Lpool, M.R C O G
TUTOR IN OBSTETRICS

UNIVERSITY OF LIVERPOOL

IT is claimed that hydrogenation of the alkaloids of ergot deprives them of their oxytocic and vasoconstrictor properties and endows them with spasmolytic ones (Stoll 1953) with the result that they bring about decreased vascular tone, active vasodilatation relaxation of the uterus and inhibition of the action of the common oxytocics including that of ergot itself It is also reported that the hydrogenated alkaloids have a latent capacity for neutralising the effect of adrenaline and noradrenaline These claims among others are made more specifically for the combination of alkaloids marketed under the trade name of 'Hydergine'* (Stoll 1953) They are to some extent substantiated as regards various animals but, except for the relief of hypertension, have not received confirmation in man

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* Hydergine contains the dihydro derivatives of ergocornine ergocryptine and ergocristine in equal proportion Supplies for this trial were provided by Sandoz Products Ltd

An earlier and somewhat similar preparation, dihydro ergotamine, was first reported by Gill and Farrar (1951) to have a favourable effect on human uterine action, promoting relaxation of the cervix and lower segment and quickening labour without danger to mother or fœtus This was confirmed by Gill (1953), Baskin and Crealock (1951), Hallum (1952), and Richardson (1952) Jeffcoate (1952) and Mori (1952), however, drew attention to the fact that dihydro ergotamine could produce uterine colic similar to that produced by the untreated ergot alkaloids, and warned of its danger to the fœtus This unfavourable effect was also reported by Altman et al (1952) and by Gill (1953)

The original users of dihydro-ergotamine did not control their observations, and they used it intramuscularly in divided doses In our trial (Jeffcoate et al 1953) better standardisation and control of dosage were obtained by administering dihydro ergotamine in dilute solution by intravenous drip, and records of uterine action were obtained by means of the Lorand tocograph In both normal and incoördinate labour no effect was observed on uterine action or on the course of labour when the dose was small Indeed, the only effect ever recorded (and that when the dose was increased) was an oxytocic one with a tendency to produce uterine colic much the same as that produced by the untreated ergot alkaloids

Hydergine was first used in the obstetric field by Wilhelm (1951), who reported that it had a beneficial effect in "secondary uterine inertia" He also claimed (though without giving comparable figures for untreated patients) that it considerably shortened the first stage of labour when administered routinely to primigravidæ Law (1954), however, reported the results of a controlled investigation in which he did not find any shortening of the first stage of labour from routine use of hydergine in primigravidæ

Our trials of hydergine on women in labour were made in 1953 and 1954

Materials

NORMAL LABOUR

Intravenous Hydergine

In a preliminary trial 5 primigravidæ, all in apparently normal labour, were treated with hydergine by intravenous drip Hydergine 0 6 mg was added to 1 litre of 5% dextrose, and the drip was started very slowly Thereafter the rate of flow was cautiously increased so long as no untoward effect was observed The clinical effect was assessed by observation of the frequency and character of the uterine contractions and of the site and intensity of the referred pain

Clinical observations were supplemented by the use of a Lorand tocograph This machine has obvious limitations but does permit comparative studies of gross changes in uterine action In assessing the tocographic records from these and other patients in the investigation hydergine was considered responsible for a change in the pattern of uterine activity only when the change followed within 15 minutes of starting the hydergine or changing the rate of its administration

Intramuscular Hydergine

The 109 patients in this part of the inquiry were primigravidæ in normal labour at term, and were unselected apart from the exclusion of cases of disproportion, 59 were treated, and 50 acted as controls Their labours were managed according to the routine practice of the hospital, hence they all received intramuscular morphine gr ¼ and pethidine 0 1 g when the cervix reached 2–3 fingers' dilatation The "treated" patients, however, were also given intramuscular hydergine, the first injection being given at the same time as f the morphine and pethidine The whole course d of four injections of 0 15 mg each at hourly intervals, but the course was not completed if full cervical dilatation intervened

The treated patients had been in labour for an average of 10 hr 6 min at the start of hydergine therapy, the corresponding time for the controls at the time observation was started was 10 hr 20 min The similarity of these figures testifies that the two groups were comparable.

INEFFICIENT UTERINE ACTION

In this group there were 17 patients (15 primigravidæ and 2 multiparæ) in whom, because of faulty uterine action, the first stage of labour was not progressing smoothly, and the standard treatment with morphine and pethidine had not had any noticeably good effect. 8 of the women had already been in labour for more than 24 hours when hydergine therapy was started Abnormal uterine action was diagnosed in the other 9 on the bas of clinical or tocographic evidence, or both, even though labour had been in progress for less than 24 hours

Uterine inefficiency was classified according t Jeffcoate et al (1953) as follows

	No of ca
Asymmetrical uterine action	1
Colicky uterus	3
Hypertonic lower segment	10
Hypotonic inertia	2
Cervical dystocia	1

All these patients were given intravenous hyderg by drip infusion In 12 of the cases uterine action bef and after treatment was studied with the Lor tocograph

These cases were not controlled by a similar gr in which no treatment was given, because severe undisputed uterine inefficiency does not occur of enough to allow this to be done within a reasonable ti Moreover, individual cases of faulty uterine action are different from each other, and the diagnosis depends much on personal opinion, that it is doubtful whet any two series can ever be truly comparable

HYDERGINE AND OXYTOCIN †

This small group is included because of the cla previously referred to, that hydergine can either neutra or inhibit oxytocics It consists of 4 primigravidæ gi hydergine intravenously while receiving oxytocin intravenous drip 3 for the induction of labour, and for hypotonic inertia in labour

Results

NORMAL LABOUR

Intravenous Hydergine

All the 5 patients in this group were ultima delivered vaginally 4 spontaneously, and 1 with forc The placenta was delivered normally and quickly in case, but in 3 the uterus remained hypotonic for time afterwards and its response to intravenous e metrine was sluggish 2 of these patients incurre blood-loss of 16 fl oz in the third stage and postpa period, and the other 12 fl oz

In 3 patients the site and intensity of the labour p remained unchanged after the introduction of hydr therapy, but in the 2 others the treatment seeme cause a considerable increase in the amount of experienced In these latter 2 and in 1 other cas tocographic records suggested that hydergine had oxytocic effect (fig 1) In only 1 patient did tocogr suggest a reduction in uterine activity, and this foll the infusion of 0 15 mg in only 7 minutes

Intramuscular Hydergine

Length of first stage —Patients in both the treated control series had been a similar time in labour observation or treatment was started From then

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† The preparation used in this series was 'Pitocin' (Park & Co) in a strength of 5 units per litre of 5% dextro

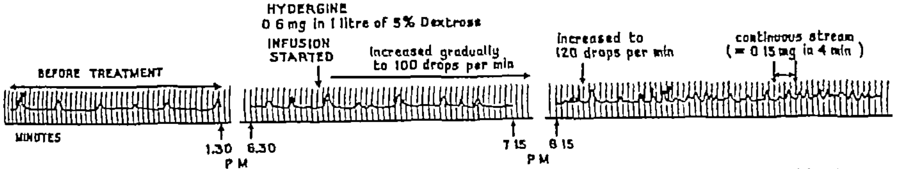

Fig 1—Record of uterine activity during successive changes in rate of hydergine drip infusion (primigravida in normal labour)

the end of the first stage of labour the average time was 5 hr 45 min in the treated and 5 hr 20 min in the untreated The average duration of the whole first stage in the two groups was thus 15 hr 51 min and 15 hr 40 min. The difference is insignificant Tables I and II show that the similarity of the two groups persists even when the figures are subdivided to show the relative lengths of the early and late parts of the first stage In general, the total duration of the first stage was proportional to the length of time taken to reach 2–3 fingers dilatation and this was true irrespective of treatment In other words when the cervix was dilating slowly it continued to do so despite treatment and the only possible effect of hydergine noted was to quicken the first stage slightly in those cases where it was already proceeding rapidly

Length of second stage—The second stage lasted an average of 50 min. in the treated patients and 48 min the controls.

Method of termination of labour—In 2 of the hydergine treated patients forceps delivery was undertaken hile there was still a narrow rim of cervix present his was because in 1 case the cord prolapsed and in the ther case hæmorrhage and signs of fœtal asphyxia sulted from premature separation of the placenta further patients in the treated group were delivered ith forceps for the following reasons

	No of cases
Failure of voluntary effort	2
Deep transverse arrest	4
Prophylactic	5
Intrapartum hæmorrhage	1
Fœtal distress	5

f the 7 cases of forceps delivery in the controls 4 were prophylactic and 3 were for fœtal distress Forceps livery took place more often in the treated group %) but it is doubtful how much importance to tach to the difference in interference rates because the beral use of forceps by some members of the staff could fully explain coincidental differences of a high magnitude

BLE I—PRIMIGRAVIDÆ IN NORMAL LABOUR WHO RECEIVED INTRAMUSCULAR HYDERGINE

ours in labour before mmencing treatment in reaching 2–3 fingers dilatation)	Time taken to complete dilatation (hours after start of treatment)					
	0–4	4–8	8–12	12–16	16–20	More than 20
8 (18 patients)	16	3	1			
16 (18 patients)	13	0	4	1		1
re than 16 (11 patients)	4	2	3		1	2

BLE II—PRIMIGRAVIDÆ IN NORMAL LABOUR (UNTREATED)

urs in labour before rt of observation (i e reaching 2 3 fingers' dilatation)	Time taken to complete dilatation (hours after start of observation)					
	0–4	4–8	8–12	12–16	16–20	Over 20
8 (22 patients)	13	7	1			1
16 (19 patients)	9	6	4			
re than 16 (9 patients)	3	3	1	1	1	

In the hospital in question the forceps rate among all primigravidæ is 18%

Third stage and immediate postpartum period—Manual removal of the placenta was not necessary in any patient, treated or untreated The placenta was always delivered within 25 min and usually within 10 min of delivery of the baby According to the routine practice of the hospital all the controls and 40 of the treated had an intramuscular injection of ergometrine 0 5 mg on completion of the third stage The 10 other hydergine treated patients had 10 units of intramuscular oxytocin The average blood loss incurred by the controls during and after the third stage was 7 fl. oz In the treated patients who were given ergometrine the loss averaged $7^3/_4$ fl. oz and in those who had pitocin 12 fl oz 8 treated patients lost more than 20 fl oz and 2 required transfusions of blood or plasma substitute Of the controls 3 bled more than 20 fl oz and 1 required transfusion Again the differences are insignificant

Fœtus—Fœtal asphyxia before delivery was evident in 7 of the treated cases and in 3 of the controls In 2 of the treated, however it was explained by retroplacental hæmorrhage Neonatal asphyxia sufficient to excite comment developed in the babies of 17 treated mothers and 24 controls The number of cases causing anxiety on the part of the attendants was 3 in the treated group and 4 in the controls Among the treated cases there were 3 stillbirths, but 2 of these were explained by accidental antepartum hæmorrhage which though not clinically evident during labour gave proof of its occurrence by the presence of old clot on the maternal surface of the placenta

INEFFICIENT UTERINE ACTION

Length of First Stage

In 15 of the 17 patients in this group the cervix was less than 3 fingers dilated at the start of the hydergine therapy In the 2 other cases the dilatation was stationary at the 4 fingers stage The cervix became fully dilated in all cases but in 1 which was classified as cervical dystocia no change took place until the resistance of the external os was overcome by digital stretching whereupon dilatation proceeded quickly The longest interval from the start of hydergine therapy to full cervical dilatation was $7^1/_2$ hours

Method of Delivery

2 patients were delivered by cæsarean section 1 was a primigravida aged 35 with a small pelvic outlet in whom a trial of forceps was abandoned The other was a primigravida whose pelvic cavity was smaller than was originally thought and the presenting head did not descend low enough for safe forceps delivery

10 patients had spontaneous deliveries and 4 were assisted with forceps The remaining case was one of twins the first fœtus having assisted breech delivery and the second being extracted with forceps

Sensation of Pain

There were 9 patients in whom low back pain was excessive and after the administration of hydergine this pain was increased in severity in 5 unchanged in 3 and relieved in 1 Another patient who complained of severe

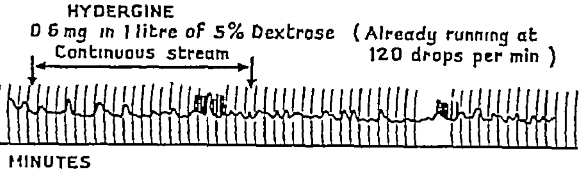

Fig 2—Record of uterine activity during rapid infusion of hydergine (primigravida with inefficient uterine action)

hypogastric colic, suffered a sharp exacerbation when hydergine treatment was begun The 6 women whose pain was increased had to be given pethidine intravenously

Tocographic Evidence

Tocographs were obtained before and after treatment in 12 cases In 5 the base line, the frequency and amplitude of the contractions, and the general pattern of the tracings underwent a change which indicated an increase in uterine activity (figs 2 and 3) In 2 patients a reduction in uterine activity was recorded, and in the remaining 5 there was no change

Third Stage and Postpartum Period

Uterine atony during the third stage and immediate postpartum phase was observed in 2 patients who lost 26 fl oz and 27 fl oz of blood In all the others uterine action was satisfactory during this period, and the placenta and membranes were delivered without event

Fœtus

Signs of fœtal asphyxia were observed at the end of the first stage of labour in 1 case, but this infant was subsequently found to have a minor degree of exomphalos In 1 other case a mild degree of neonatal asphyxia developed but required no special treatment There were no stillbirths or neonatal deaths

OXYTOCIN-INDUCED UTERINE CONTRACTIONS

The 4 women in this group were all receiving an oxytocin drip infusion for the purpose of inducing labour or treating hypotonic inertia Hydergine was added to the drip when uterine contractions were strong and regular In 2 cases hydergine appeared to increase the frequency and strength of the contractions (fig 4) and the intensity of the patient's pain A modified oxytocic effect was also suggested in the tocograph of the third patient the effect of oxytocin was accentuated while the hydergine was introduced at the rate of 90 drops a minute, but, when the infusion was increased to a continuous stream, the contractions were reduced in amplitude but not in frequency In the remaining case the oxytocin induced contractions were less intense after the introduction of the hydergine

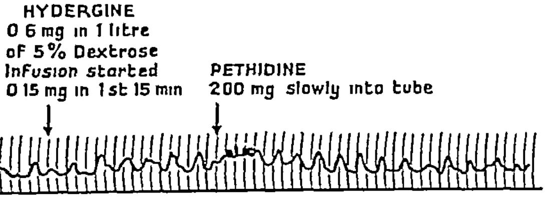

Fig 3—Record of uterine activity during rapid infusion of hydergine (primigravida with inefficient uterine action)

Incidentally, the 3 women who were receiving oxytocin with the object of inducing labour did not enter labour, contractions dying away as soon as the drip was discontinued A combination of oxytocin and hydergine given by repeated intramuscular injections was tried as a of inducing labour in 6 further women and it ısuccessful in all

Discussion

The almost identical progress of treated and untreated women in normal labour confirms the findings reported by Law (1954) and indicates that no advantage is to be gained from the routine administration of hydergine, which does not materially influence the speed and smoothness of the first stage Moreover there is nothing to support the idea that hydergine favours relaxation of the cervix and lower segment

As regards inefficient uterine action the findings were inconclusive, if only because the assay could not be controlled The fact that all the patients reached full cervical dilation in less than 7½ hours after the start of treatment at first suggests that hydergine may have had some effect on the labours However, such an interpretation is open to question, since many of the patients had large amounts of pethidine—usually intravenously—for the relief of their intense pains, and it is known that pethidine sometimes exerts a corrective effect on the disorderly uterus

If it is concluded that hydergine did quicken some, if not all, of the labours, the evidence suggests that it usually did so by exerting an oxytocic action rather th by reducing hypertonus There were only 2 women whom it may have had a quietening and regulating effe on uterine behaviour

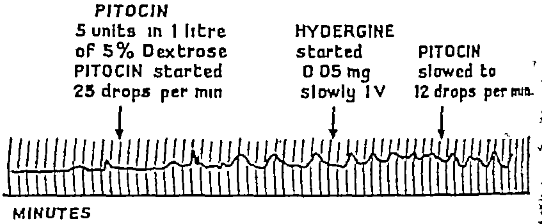

Fig 4—Record of uterine activity under influence of oxytocin alone of oxytocin and hydergine simultaneously (primigravida under oxytocin induction of labour)

The failure of hydergine to inhibit contractions induce with oxytocin, and the finding that in some cases it act synergistically rather than antagonistically, are keeping with this conclusion

A possible inhibitory action of hydergine is suggeste by the tendency to uterine relaxation and hæmorrha during and after the third stage in women who h received intravenous hydergine This observation, ho ever, may be better explained by the withdrawal of oxytocic action when the drip was discontinued at time of full cervical dilatation Moreover a simil phenomenon is reported when ergometrine or other er alkaloids are used intravenously during labour ra than being reserved until delivery is complete (Bick 1943, McConnell and Schauffler 1943)

If the only demonstrable effect of hydergine is an ox tocic one, it may well be that, like dihydro ergotami it can induce hypertonus when given in large do The tocographic records suggested such an effect some patients, but in none did it develop to a se degree or threaten the life of the fœtus It ther seems that its oxytocic action is not so strong or danger as that of dihydro ergotamine, and the same is true of alkaloids from which each is derived

Conclusion

Despite laboratory evidence to the contrary, the re of this clinical investigation indicate that the hydr genation of the ergot alkaloids does not deprive th of their oxytocic action, let alone reverse it The pe tence of this property means that their use involves which is not compensated by any other demon effect on uterine efficiency.

References at foot of next column

THE URICOSURIC ACTION OF ETHYL BISCOUMACETATE

R Sougin Mibashan *
B Sc., M.D Cape Town
C.S.I.R. RESEARCH BURSAR AND 1955 NUFFIELD DOMINION FELLOW IN MEDICINE

M. Horwitz
B.Sc., M.D Cape Town M.R C.P
PHYSICIAN IN CHARGE OF THE ARTHRITIS CLINIC GROOTE SCHUUR HOSPITAL, CAPE TOWN

From the Department of Medicine Groote Schuur Hospital and University of Cape Town

Of all mammals only man, apes, and the dalmatian coach hound excrete substantial amounts of uric acid in the urine In man the renal mechanism of excreting uric acid consists in complete filtration of plasma urate by the glomeruli and active reabsorption of about 90% by the proximal tubules (Berliner et al 1950) the net clearance of urate is thus reduced to but a tenth of the glomerular filtration rate Drugs which increase the excretion of urate—e.g , salicylate, cinchophen probenecid ('Benemid'), phenylbutazone, and cortisone—do so by impairing its active reabsorption by the tubules and thereby increasing its renal clearance (Beyer et al 1951 Berliner 1954) These and similar substances are called uricosuric agents, of which some occupy an important place in the modern management of gout

The biochemical processes in the tubule cell with which they interfere are far from elucidated but a relationship exists (Talbott 1943 Beyer et al. 1951) between the reabsorption of urate and the active tubular secretion of certain other organic molecules—e.g phenol sulphonphthalein (P.S.P) *p* aminohippurate (P A.H), *p*-aminosalicylate (P A.S), diodone, and penicillin (fig 1) The cellular transport mechanism for reabsorbing urate thus shares one or more steps with the tubular secretion of these foreign compounds Loading the tubules with one of these substances will competitively depress the passage of any of the other members of the group For example P.A H. depresses the secretion of penicillin and P.S P the reabsorption of urate Similarly agents which are not secreted but appear to block some phase in the enzymatic transport process—e g carinamide and probenecid—will impair the tubular passage of any of the foregoing compounds. Probenecid was first used like its less well tolerated precursor carinamide for maintaining the blood levels of penicillin and P A.S by inhibiting their renal tubular secretion The further ability of carinamide and probenecid to impair the reabsorption of urate was first applied by Wolfson et al (1948) and Gutman (1951) to the uricosuric treatment of gout.

Probenecid (Gutman and Yü 1951 Horwitz and Sougin Mibashan 1953, 1955) and salicylate (Marson 1953) are currently the most effective uricosuric drugs for prolonged use Of the two probenecid has the advantages of great potency in small dosage (0 5–1 5 g daily) and negligible toxicity and its biochemical and clinical effectiveness are relatively preserved even in the presence of renal disease (Sougin Mibashan 1954)

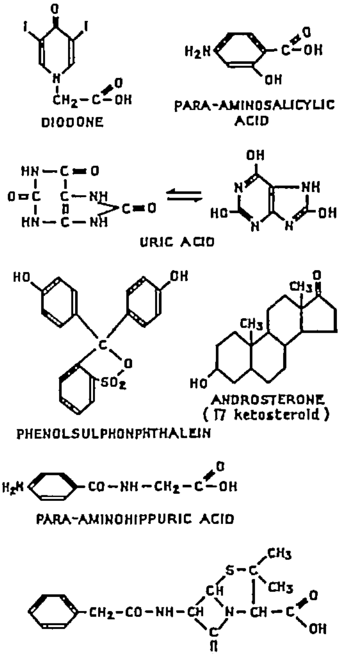

Fig 1—Compounds sharing the same system of renal tubular transport.

Discovery

Ethyl biscoumacetate ('Tromexan') is a synthetic anticoagulant introduced a few years ago for the clinical management of thrombo-embolic disease Compared with the closely related dicoumarol, it has the advantages of speedier increase in the prothrombin time and quicker return to normal when it is withheld A typical effective single oral dose in man is 1 5 g making it about a fifth as potent as dicoumarol (Wright 1952) The uricosuric properties of ethyl biscoumacetate were first observed in the following circumstances

Gout is common in Cape Town, hundreds of cases having been observed among its half million people in the past few years. Clinical and metabolic studies of the continuous use of probenecid in fifty cases of gout for 6–30 months have been reported by Horwitz and Sougin Mibashan (1953 1955) During these studies a certain patient (case 82 of our series) was admitted to hospital for clinical assessment In addition to the recent onset of episodic arthritis, which responded to colchicine and with which there was hyperuricæmia he also had symptomless auricular fibrillation. There was no other clinical or cardiographic evidence of heart disease and it was decided to treat him with quinidine to correct the arrhythmia. As the arrhythmia was presumably of long duration anticoagulant measures were taken as well guided by daily prothrombin estimations.

After a day or two of treatment with quinidine and ethyl biscoumacetate it was observed from serial urate determinations that the patient was no longer hyperuricæmic (fig 2) When the drugs were discontinued because of failure to restore normal rhythm the serum urate rose to its former high level Simultaneously less urate was excreted, and the urinary urate/creatinine ratio decreased

This coincidence of events prompted treatment with ethyl biscoumacetate alone The metabolic results (fig 2) were indistinguishable from those which might have been produced by a potent uricosuric agent such as probenecid. Fig 3 illustrates the effect of ethyl bis

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At present at Hammersmith Hospital, London

PROF JEFFCOATE DR. WILSON: REFERENCES

Altman, S G., Waltman R. Lubin S Reynolds, S R. M. (1952) Amer J Obstet Gynec 64 101
Baskin M J., Crealock, F W (1951) Rocky Mtn med. J 48 514
Bickers W (1942) Amer J Obstet. Gynec 46 238
Hill, R. C (1953) J Obstet Gynaec., Brit Emp 60 104
— Farrar J M. (1951) Ibid 58 79
Hallum, J (1952) Ibid 59 656
Jeffcoate T N A (1952) Ibid, p 658
— Baker, K Martin, R. H (1952) Surg Gynec Obstet 95 257
Law R G (1954) J Obstet Gynaec., Brit Emp 61 581
McDonell C Schauffler G C. (1943) West J Surg 51 402.
Moir J C. (1952) J Obstet Gynaec Brit Emp 59 661
Richardson K S (1952) Ibid p 653
Roll, A (1953) Indian J Pharm. 15 200
Wilson, E (1951) Klin Med 6 414

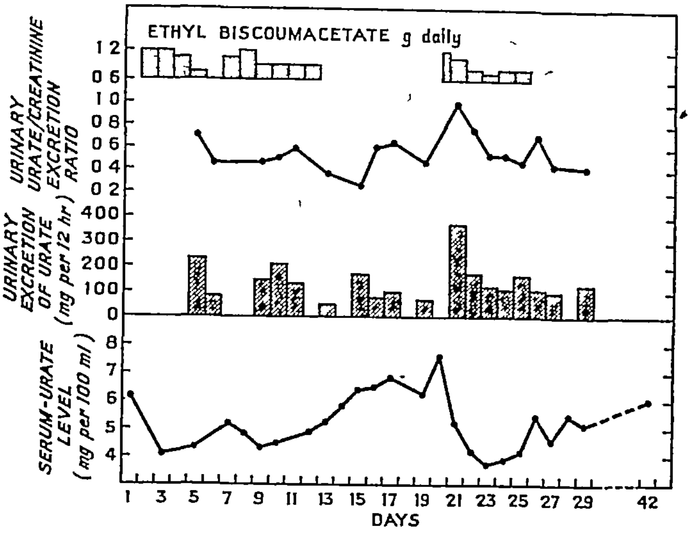


Fig 2—Effect of ethyl biscoumacetate in case 82 (gout)

coumacetate given for 10 days to another gout patient (case 8), followed several weeks later by probenecid therapy This patient had chronic renal disease with a serum-urea level of nearly 100 mg per 100 ml The uricosuric response of a falling serum urate level and rising urinary excretion of urate occurred with both drugs There was no clear relationship, during treatment with ethyl biscoumacetate, between either the serum-urate level or the urinary output of urate and the daily prothrombin value

Confirmatory Experiments

MAN

Effect of Single Oral Dose of Ethyl Biscoumacetate on Serum urate Level

Four gout patients, three patients with coronary disease without overt cardiac or renal failure, one orthopædic patient in good general health, and one normal subject were each given either 1 2 or 1 5 g of ethyl biscoumacetate in one oral dose The serum-urate level was measured, by the method of Herman Brown (1945), before the drug was given and one or more times in the succeeding 24 hours The results are illustrated in fig 4, the lowest serum-urate level after the administration of ethyl biscoumacetate being used Prothrombin-times were measured by Quick's one stage method before and after the administration of ethyl biscoumacetate

In every instance there was an impressive fall in the serum urate level, ranging from 40% in the normal subject to 12% in one of the gout patients (a woman with severe hypertension and slight renal impairment) Case 8, with tophaceous gout and severe renal disease, showed a 22% fall The earliest clear cut reduction was found 1–2 hours after the administration of ethyl biscoumacetate, and the greatest fall after 5 hours in two subjects observed at short intervals, in these people the prothrombin time did not lengthen until next day

Effect of Ethyl Biscoumacetate on Renal Clearance of Urate and on Urate/Creatinine Clearance Ratio

Methods—Clearance experiments were done under standard conditions, in the morning, at rest, and after liberal hydration and a snack breakfast Spontaneously voided urine was collected at carefully timed intervals of about 30 minutes When clearance collections were continued for many hours, as in R S M and case 12, the periods were sometimes longer Patients were instructed in the technique of emptying the bladder, and the first collection was usually regarded as a practice one Subjects apparently lacking satisfactory control of their bladders were excluded To obviate changes in clearance of urate at small flows of urine (Brochner Mortensen 1940), collections of less than 2 ml per min (rare with good hydration) were not used In both serum and urine the amount of urate was determined by Brown's (1945) method and of creatinine by the method of Bonsnes and Taussky (1945) No intravenous priming being used, the clearance values represented the endogenous chromogens Venous blood was drawn usually every clearance period, but in longer experiments a serum determination sometimes served its own and the succeeding period The clearance of endogenous creatinine is in accepted use as an expression of glomerular filtration rate (G F R.) in man and dog (Homer Smith 1951) Standard values in man for a body surface area of 1 73 sq m are about 10 ml per minute for urate clearance, and 127 and 117 ml per minute for G F.R. in men and women respectively (Gutman and Yü 1951, Homer Smith 1951)

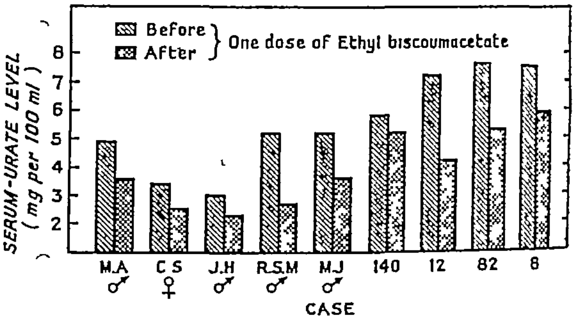


Fig 4—Effect of single oral dose of ethyl biscoumacetate on serum-urate level in 5 non-gouty and 4 gouty persons.

Results—The effect of ethyl biscoumacetate on the urate/creatinine clearance ratios of four gout patients and one normal is shown in fig 5 In case 82 the clearance tests were done a week apart,

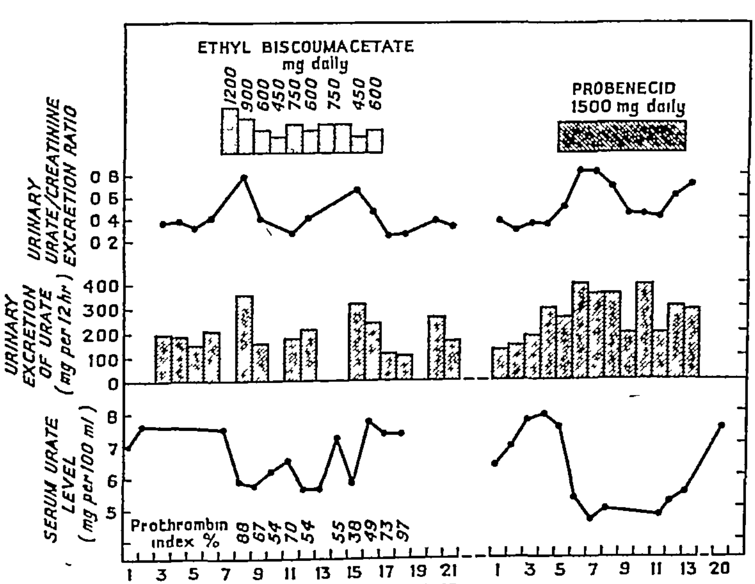


Fig [illegible] of ethyl biscoumacetate, and subsequently probenecid, in case 8 (gout with chronic renal disease)

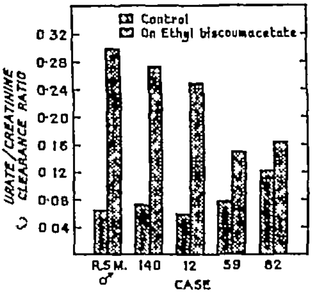


Fig 5—Effect of single oral dose of ethyl biscoumacetate on urate/creatinine clearance ratio in 1 normal subject and 4 patients with gout.

the second during a course of treatment with ethyl biscoumacetate. All the others had clearances done for several successive periods immediately before and after one oral dose of ethyl biscoumacetate The smallest dose was 1 2 g (case 140) and the largest 1 8 g (R. S M.) The histograms in fig 5 represent the average clearance values of 2–4 collection periods before the ingestion of ethyl biscoumacetate and 3–10 collection periods following the drug The rise in urate clearance and hence in the urate/creatinine clearance ratio is impressive the latter increasing by as much as 370% in one case The G.F.R underwent no significant change

The accompanying table shows the detailed results obtained in R S M. and case 12 each of whom had a diurnal series of clearance determinations with the following noteworthy observations

(1) The first steep rise in urate clearance took place less than 2 hours after the administration of ethyl biscoumacetate denoting a lag of 1–2 hours after ingestion before a uricosuric effect was produced. This is the time known to be taken for the absorption of ethyl biscoumacetate (Brodie et al 1952)

(2) The greatest increase in urate/creatinine clearance ratio attained in any single period was 480% (0·064–0 309) and 660% (0 038–0 ·60)

(3) A significant increase in urate clearance preceded the first distinct fall in serum urate level in keeping with a renal site of uricosuric action.

EFFECT OF ETHYL BISCOUMACETATE ON RENAL CLEARANCE OF URATE AND ON URATE/CREATININE CLEARANCE RATIO IN ONE NORMAL AND ONE GOUT SUBJECT

Subject	Time (min)	Urine flow (ml. per min)	Creatinine		Urate		Urate/creatinine clearance ratio	Prothrombin index (%)
			Serum level (mg per 100 ml)	Clearance (ml per min)	Serum level (mg per 100 ml)	Clearance (ml. per min.)		
R S M : Ethyl biscoumacetate 1 8 g ingested at +7 min. oral hydration throughout	−172	2 45	1 ·6	104	5 15	8 20	0·078	
	−88	10 00	1 10	113	5 00	7 9	0·055	100
	−38	16·00	1 16	126	4 35	7 70	0 057	100
	0–30	10 08	1 11	11	4 ·6	9 26	0·079	
	40–118	1 48	1·00	128	4 30	37 5	0··93	
	119–·31	1·00	1 ·0	101	4 32	35 2	0 330	100
	·35–308	4 26	1 11	141	2 83	60 4	0 358	100
	309–367	6 18	1 20	101	· 7	34·0	0 337	
	368–418	2 27	1 20	109	2 7·	40 2	0 368	
Case 12 : Ethyl biscoumacetate 1 5 g ingested at +4 min. oral hydration throughout	−106	8 30	0 91	131	7 ·0	7·03	0 054	
	−70	7 10	0 88	1·6	10	8 80	0·070	100
	−35	11 10	0 93	131	6 05	6·65	0 051	
	0–39	11 30	0 89	157	6 90	8 90	0·057	
	40–·8	3 65	0 88	137	6 80	11 40	0·083	
	79–114	10 40	0 91	102	6 ·0	35·0	0 216	
	115–148	1·50	0 75	178	5 60	46 0	0 258	
	149–184	8 65	0 75	140	5 60	29·0	0 ·07	100
	1··– ·21	8 63	0 80	140	6·00	26 3	0 188	
	222–255	14 00	0 90	142	4 50	76 1	0·535	
	·56–·90	1· 30	1·02	118	4 13	66 0	0 560	
	300–344	3 78	1·0·	105	4 13	19 2	0 178	

(4) Early slight loss of serum urate unassociated with increased clearance was detectable apparently as a result of copious diuresis.

(5) Prothrombin activity stayed at 100% when the urate clearance had already greatly increased In this and other experiments the impairment of prothrombin after one dose of ethyl biscoumacetate was first detected after the serum urate had already begun to return to normal, usually on the day following the administration of ethyl biscoumacetate. This conforms to the recognised lag in the anticoagulant effect of ethyl biscoumacetate in clinical use

RAT

The main end product of purine metabolism in mammals other than primates and the dalmatian dog is allantoin which is derived from its precursor uric acid by the action of uricase, an enzyme present mainly in the liver Uric acid in the blood and urine of most mammals exists therefore by virtue of not yet having undergone complete uricolysis and its concentration in both is accordingly low Its renal excretion though small appears to follow a pattern of filtration and partial reabsorption essentially similar to that observed in man (*Byers et al* 1947)

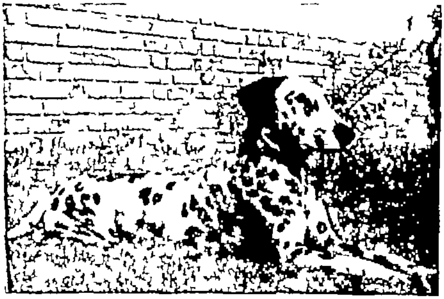


Fig 4—Dalmatian coach-hound.

Ethyl biscoumacetate given by mouth to fourteen rats and probenecid given by mouth to fourteen other rats produced similar uricosuric effects. Serum urate and urine urate levels were measured in hourly samples collected for 2 hours before and 5 hours after the giving of each drug In each case the level in the urine rose and that in the serum fell offering further evidence of the similarity of the actions of ethyl biscoumacetate and probenecid

DALMATIAN COACH HOUND AND MONGREL DOG

The singular spotted appearance of the dalmatian breed (fig 6) is genetically correlated with a unique pattern of urate metabolism (Friedman and Byers 1948 Wolfson et al. 1950)

(1) The urine contains large amounts of urate and relatively little allantoin

(2) The urinary excretion of urate is disproportionately large compared with that in man and is accomplished at a much lower plasma urate level—i.e the renal clearance of urate is very high.

(3) The high clearance is due to a renal tubular anomaly whereby urate is not reabsorbed from the glomerular filtrate The body therefore loses urate that would have been converted to allantoin, the formation and excretion of which are consequently diminished The low output of allantoin may in addition partly be due to lessened activity of hepatic uricase (Friedman and Byers 1948)

(4) The demonstration (Wolfson et al. 1950 Beyer et al. 1951) that the clearance of urate in the dalmatian exceeds the G.F.R indicates not merely a failure of reabsorption but also active tubular secretion contributing to the high renal clearance of urate

(5) Uricosuric agents which act by impairing reabsorption of urate are ineffective in the dalmatian, this process being absent (Miller et al 1951, Beyer et al 1951) As might be expected if urate is actively secreted by the tubules, Beyer et al (1951) further observed that the urate/creatinine clearance ratio (greater than 1 0 in the dalmatian) was not only not increased when probenecid was given, but even was diminished, while the plasma urate level rose slightly

This inverted response by the dalmatian to uricosuric agents, resulting from its reversed renal tubular transport mechanism for urate, enables this animal to be used for pin-pointing the renal site of action of a uricosuric drug The following experiments show that ethyl biscoumacetate is uricosuric in the mongrel dog, confirm the active tubular secretion of urate in the dalmatian coach-hound, and establish the action of ethyl biscoumacetate as a transport inhibitor able to impair the passage of urate in either direction through the renal tubule cell.

Methods

The mongrel was a healthy adult female weighing 18 kg, and the dalmatian a pure bred young male weighing 16 kg Both were kept on a normal balanced diet except for deprivation of solid food for 15 hours before each experiment The dogs drank water freely before the tests, and were given half a litre by stomach tube during the 2 hours before clearance collections began To ensure adequate diuresis and to provide a route for administering drugs, 0 6% saline solution was given by venoclysis at a fairly constant rate of 2 ml a minute throughout the procedure Limb veins were entered percutaneously with a 20 gauge short-bevel Luer Lok needle attached to an infusion set Light anæsthesia was maintained with pentobarbital sodium, 20 mg per kg body-weight, given intraperitoneally, with small intravenous additions as required A series of endogenous urate and creatinine clearances was determined for each dog before and after the intravenous administration of probenecid and ethyl biscoumacetate, intervals of at least a week separating the administration of the two drugs in each dog Though analytical quantities of urate and creatinine would have been enhanced by priming with these substances, avoidance of the exogenous technique carried the advantages of simplicity, greater freedom in the duration of clearance periods and in the timing of mid point blood samples, greater freedom in the rate of flow of the intravenous infusion, and absence of possible reactions to alkaline solutions of urate

Each experiment comprised 9–14 clearance periods extending over 5 or more hours Urine was collected at carefully timed intervals through an indwelling catheter with the aid of suprapubic pressure and air displacement Blood samples for urate, creatinine, and prothrombin estimations were obtained by direct puncture of limb veins other than the one being infused, because of the low serum levels of both chromogens the mean of several values before and after administering each drug was used in calculating all the clearance figures in a particular experiment

Intravenous administration of both test agents was desirable in these series of short term clearances Solutions of ethyl biscoumacetate and probenecid (both weak acids), containing 1000 mg in 20 ml, were prepared by extraction from the crushed tablets with equivalent proportions of warm dilute NaOH, and filtering The pH of the solution was adjusted to neutrality short of precipitating the free compound, and sterilised through a Seitz filter After several control clearance collections the drugs were given by injection of half the chosen dose and infusion of the remainder at the drip rate The mongrel received 60 mg of probenecid per kg of body weight in the first experiment, and 45 mg of ethyl biscoumacetate per kg of body weight in the second In the absence of mishap with the mongrel, the dalmatian was given twice the amount of each drug to facilitate the more difficult detection of a possibly lowered urate/creatinine clearance ratio

Results

The results are summarised in fig 7 In general, excellent urine flows were maintained during the clearance procedures, and the G.F.R remained relatively constant

Mongrel —The injection of probenecid was associated with a striking uricosuric response Compared with the average con[illegible]es, the urate/creatinine clearance ratio increased by a [illegible] of 97% and a mean of 73% (fig 7) When ethyl biscoumacetate was given, urate/creatinine clearance was increased by a maximum of 63% and a mean of 26%. (Statistical analysis of these results by difference of means, using 'Student *t*' distribution, shows them to be highly significant at a 1% level)

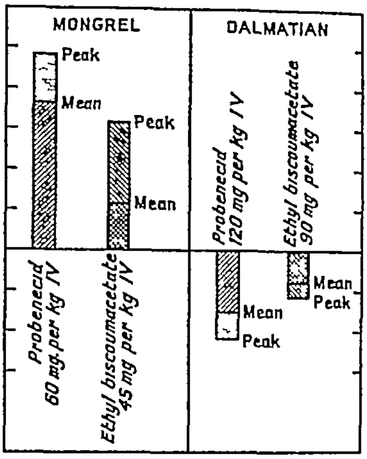


Fig 7—Effects of probenecid and of ethyl biscoumacetate on urate/creatinine clearance ratio in a mongrel and in a dalmatian dog

For both agents the increased urate clearance became apparent a few minutes after their intravenous administration, contrasting with the rather longer lag after oral dosage in man and rat Prothrombin impairment by ethyl biscoumacetate was again a later event, occurring between the 2nd and 3rd hours

Dalmation —In both experiments the normal urate/creatinine clearance ratio was substantially greater than 1 0, which supports the active tubular secretion of urate in the dalmatian. The possibility of falsely high ratios due to errors in the *absolute clearance values is offset by the further* positive action of the transport inhibitor probenecid in reducing the calculated values for urate/creatinine clearance, thus providing independent evidence of a tubular secretory mechanism.

The results confirm the action of ethyl biscoumacetate as an inhibitor of renal tubular transport of urate The urate/creatinine clearance ratio decreased from a mean control figure of 1 12 to a mean of 0 94, a 16% reduction. The greatest single reduction was 23% (After administration *of probenecid in larger dosage on a* different day the reductions were 30% and 44% respectively) Analysis of results for each experiment, using 'Student *t*' distribution, shows that, with the number of determinations involved, the results are statistically significant The smallish percentage changes should be viewed in the light of their negative direction and the total amount of urate which they represent in the dalmatian The prothrombin index was not reduced during the experiment

OTHER TUBULAR TRANSPORT FUNCTIONS

Since urate reabsorption is served by a transport mechanism which is also used for the tubular secretion of certain organic compounds (fig 1), it was desirable to know whether ethyl biscoumacetate, like other uricosuric agents, could impair the tubular transport of these substances

P A.H —The effect of ethyl biscoumacetate on the tubular transport of P.A.H was studied in a normal subject by determining the maximum tubular secretory capacity (Tm_{PAH}) before and after a single oral dose of the drug Urate and creatinine clearances were simultaneoulsy measured Fig 8 shows that Tm_{PAH} was progressively reduced, starting 1 to $1^1/_2$ hours after the dose of ethyl biscoumacetate, at the same time as urate clearance and the urate/creatinine clearance ratio increased

Penicillin —A limited investigation was made of serum penicillin levels in two men, after a standard intramuscular injection of the sodium salt given alone and during the oral administration of ethyl biscoumacetate The results suggest that ethyl biscoumacetate slightly delays the excretion penicillin, and the degree of interference if any should be further studied by penicillin-clearance techniques. Similar estimations after the administration of probenecid showed unequivocal retention of penicillin and it seems possible that ethyl biscoumacetate does not exert an effect comparable to that of probenecid on this particular tubular transport passenger

P.S.P—In another limited investigation the urinary excretion of P.S.P after a standard intravenous injection in two men, was impressively delayed up to 2 hours later when ethyl biscoumacetate was administered orally before the dye

17 Ketosteroids.—Among the properties of probenecid is the interesting ability to diminish the urinary excretion of endogenous 17 ketosteroids (Gardner et al 1951) presumably by impairment of a tubular secretory mechanism in common with the foregoing group of compounds. We have not had the opportunity to compare the effect of ethyl biscoumacetate except in one instance with negative results The problem deserves investigation, together with many others arising from the renal activities of this drug

Implications

Modification of a metabolic process by a chemical compound is always interesting When, as in the present case the observation implicates such widely separated topics as blood coagulation, the biochemistry of gout coronary atherosclerosis, hepatic and renal function, and mechanisms of rheumatic inflammation the scope for further research and correlation is unusually wide

PHARMACOLOGICAL RELATIONSHIP OF URICOSURIC, ANTICOAGULANT AND ANTIRHEUMATIC DRUGS

Ethyl biscoumacetate is not the first compound whose molecule combines uricosuric and anticoagulant properties. Salicylate and cinchophen are both potent eliminators of urate and each can impair prothrombin activity experimentally or as a clinical complication (Hueper 1946 Glazebrook and Cookson 1947) This suggests that the separate processes of urate transport by renal tubule cells and of the production of prothrombin and factor VII by hepatic cells are chemically related and may be competitively inhibited or otherwise suppressed by the same agents The delay before prothrombin time is affected after the ingestion of ethyl biscoumacetate in contrast to the early uricosuric response, seems explicable by the time required for depleting the plasma of its clotting factors Chemical interference with their enzymatic synthesis in the liver may well begin promptly after the alimentary absorption of ethyl biscoumacetate as the inhibition of renal tubular transport mechanisms appears to do

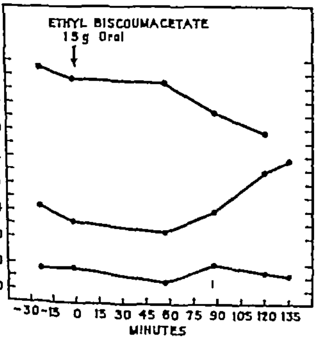


FIG 3—Renal tubular reabsorption of urate and maximal secretory capacity for P.A.H simultaneously impaired after administration of ethyl biscoumacetate. (Normal subject, primed with P.A.H at [illegible] minutes.)

The absence of manifest anticoagulant activity by uricosuric agents like probenecid and phenylbutazone and the widely varying degrees of it displayed by ethyl biscoumacetate salicylate and cinchophen, may be related to differences in their tissue distribution, solubilities excretory mechanisms, or metabolic breakdown—factors which modify pharmacological action to a high degree Moreover among the established uricosuric agents, more than one mechanism is recognised by which tubular transport may be hindered—e g cinchophen and the experimental compound dehydro acetic acid (D.H A) are inhibitors of succinic dehydrogenase (Shideman and Rene 1951) whereas probenecid is believed to block a conjugative step served by co-enzyme A (Taggart 1954) Possibly only those uricosuric agents which act at a certain point in the transport mechanism can disturb a corresponding step in the synthesis of factor VII

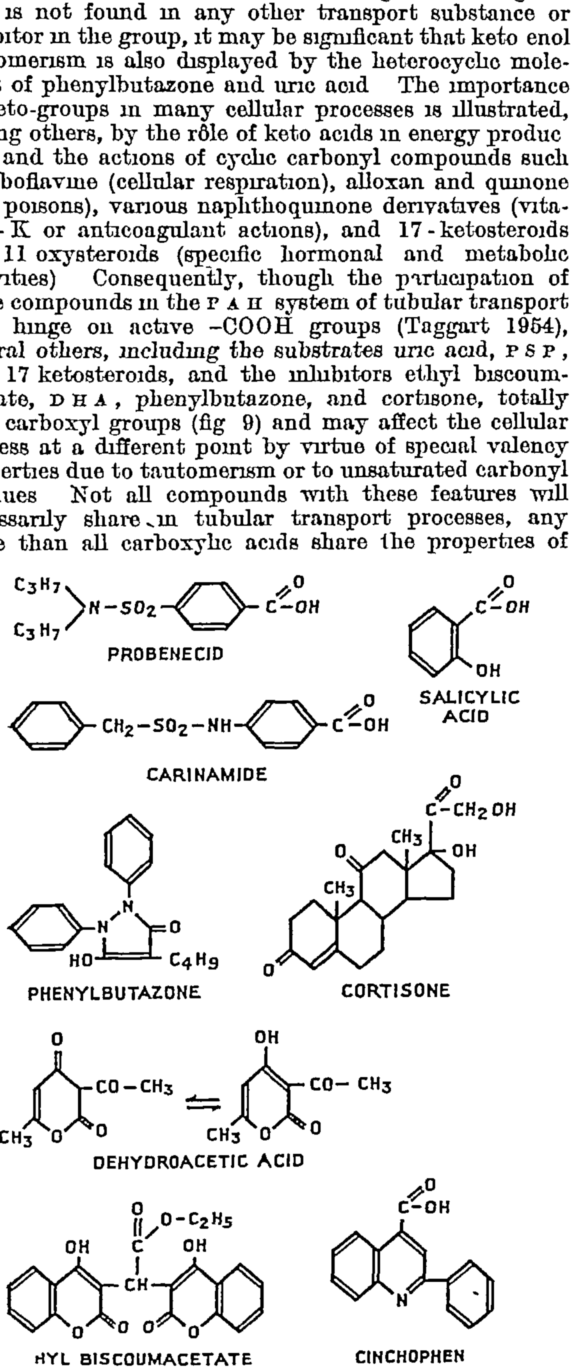
It remains to explore the truth of the latter possibility to study the effect of other coumarin compounds on renal tubular processes and to test the ability of vitamin K to protect tubular transport mechanisms against inhibition by ethyl biscoumacetate For several reasons it is conceivable that vitamin K in vivo might not necessarily oppose the renal activities of ethyl biscoumacetate in the same way as it protects the hepatic synthesis of clotting factors.

It is opportune to remark on two other significant combinations of pharmacological function One is the striking regularity with which antirheumatic or antiphlogistic drugs like salicylate, cinchophen cortisone, and phenylbutazone are simultaneously uricosuric a property discovered in each case after clinical introduction of the drug *The other concerns* several reports of the use of various anticoagulants in the treatment of acute rheumatic fever rheumatoid arthritis and gout Consistency is lacking in the premises underlying such treatment in the drugs used and in the clinical results. Howe et al (1952) were impressed by the antiphlogistic effect of heparin and its synthetic analogue Paritol in acute gout remarking that no simultaneous uricosuric effect was detected. Glazebrook and Wrigley (1949) in the light of work correlating salicylate with antihyaluronidase activity treated acute rheumatic fever with heparin (also a strong inhibitor of hyaluronidase) without special success They suggested that antihyaluronidase activity might also be a property of dicoumarol, as it is of the chemical derivative salicylate We wonder whether ethyl biscoumacetate (which functionally resembles salicylate and cinchophen in impairing prothrombin activity and, like salicylate, cinchophen cortisone and phenylbutazone, impairs the reabsorption of urate) also shares their antirheumatic and/or antihyaluronidase activity

We feel that these reflections, if somewhat ingenuous emphasise the importance of correlating biochemical knowledge in three apparently separate spheres—tubular transport of urate hepatic synthesis of clotting factors and rheumatic or gouty inflammation of connective tissue For one chemical compound to affect the function of two or more tissues (liver kidney nervous system bone marrow) is not unusual To do so not apparently by crude impairment of vital cellular activities (as occurs with many chemical poisons) but by highly selective interference with one of many cellular functions in both kidney and liver (as appears to be the case with ethyl biscoumacetate) is more remarkable

RELATION OF URICOSURIC ACTION TO CHEMICAL STRUCTURE

The difficulties of explaining the tubular transport mechanism for urate P.A.H &c in terms of molecular structure of the participants have been emphasised by Beyer (1950) Taggart (1954) and Sougin Mibashan (1954) The addition of ethyl biscoumacetate to the field does not appear to be of immediate help in identifying a particular key group determining participation in, or inhibition of, tubular transport (fig 9) The fact that compounds resembling ethyl biscoumacetate may yield salicylate on chemical degradation is of limited note, as it was in originally trying to explain their anticoagulant action (Overman et al 1944) One point of special interest, however, is the structural resemblance between part of the molecule of ethyl biscoumacetate and that of D H A , an experimentally used transport inhibitor believed to act specifically by impairing energy-production from succinate oxidation at a certain point in the mechanism (Shideman and Rene 1951) Both ethyl biscoumacetate and D.H A possess a lactone ring with a carbon residue at the 3-position and a propensity for 2, 4-keto enol tautomerism , and, though this configuration is not found in any other transport substance or inhibitor in the group, it may be significant that keto enol tautomerism is also displayed by the heterocyclic molecules of phenylbutazone and uric acid The importance of keto-groups in many cellular processes is illustrated, among others, by the rôle of keto acids in energy production and the actions of cyclic carbonyl compounds such as riboflavine (cellular respiration), alloxan and quinone (cell poisons), various naphthoquinone derivatives (vitamin - K or anticoagulant actions), and 17 - ketosteroids and 11 oxysteroids (specific hormonal and metabolic activities) Consequently, though the participation of some compounds in the P A H system of tubular transport may hinge on active –COOH groups (Taggart 1954), several others, including the substrates uric acid, P S P , and 17 ketosteroids, and the inhibitors ethyl biscoumacetate, D H A , phenylbutazone, and cortisone, totally lack carboxyl groups (fig 9) and may affect the cellular process at a different point by virtue of special valency properties due to tautomerism or to unsaturated carbonyl residues Not all compounds with these features will necessarily share in tubular transport processes, any more than all carboxylic acids share the properties of P A H or probenecid , equally important molecular factors determining solubility, distribution, breakdown, and excretion must first combine suitably to admit the compound to the renal mechanisms



suppressing the " urate-P.A.H " system of renal tubular transport.

CLINICAL APPLICATIONS

It is unlikely that ethyl biscoumacetate, whose anticoagulant properties have established it in the treatment of thrombo embolic disease, would be used in other possible rôles except in special circumstances Moreover, a potent and well-tolerated uricosuric agent like probenecid would not easily be displaced in the management of gout by any drug unless it carried distinct advantages

From our present experiments, and from many similar observations made with probenecid (Gutman and Yü 1951, Sougin-Mibashan 1954), the uricosuric potencies of ethyl biscoumacetate and probenecid appear to be roughly of the same order, 1 5 g of each producing something like a 40% fall in serum urate level and a twofold to fivefold increase or more in urate clearance If statistically valid figures supported this comparison, the greater molecular weight of ethyl biscoumacetate would give it a higher equivalent uricosuric potency than that of probenecid.

Although the use of ethyl biscoumacetate might be neat, therefore, *in treating myocardial infarction in a* gout patient, there would be practical value in finding a related coumarin compound with similar uricosuric but little or no anticoagulant activity Among the 106 coumarin derivatives originally studied by Overman et al (1944) few were effective anticoagulants Special interest attaches to their Compound 16, which was the free carboxylic acid form of ethyl biscoumacetate Unlike the currently used ethyl ester, Compound 16 lacked anticoagulant activity Its renal tubular affinities now require separate testing, with possibilities that are obvious Not only might a useful new uricosuric agent emerge but also (in the light of previous remarks) one with possible antiphlogistic properties as an added advantage in the management of gout

A final reflection concerns uric acid, coronary atherosclerosis, and anticoagulant therapy In an exhaustive study of 100 patients, aged less than 40, with coronary heart disease, Gertler and White (1954) found that serum urate levels were significantly higher than normal. An index derived from serum-urate, cholesterol, and lipid phosphorus provided better correlation with the disease than any other data Logically this implies that correction of moderate hyperuricæmia—even apart from gout—may be no less important, in the prevention or management of coronary atherosclerosis, than controversial attempts to lower the serum cholesterol level.

The use of coumarin anticoagulants in myocardial infarction has been justified mainly by statistical evidence that mortality and complications are reduced (Tulloch and Gilchrist 1951) Though such therapy is currently controlled in terms of blood coagulability, there is no proof that the clinical results are directly due to diminished prothrombin activity The discovery that ethyl biscoumacetate has a distinct additional action on uric acid—a substance implicated independently in coronary heart disease—may widen the present concept of modern anticoagulant therapy

Summary

The anticoagulant drug ethyl biscoumacetate (' Tromexan ') strongly enhances the renal excretion of uric acid in man, rat, and dog This uricosuric action is due as in the case of probenecid, salicylate, cinchophen, and similar agents, to reversible impairment of urate reabsorption by the proximal tubules, with consequent increase of urate clearance In this respect ethyl biscoumacetate appears, from the limited data so far obtained, to have a uricosuric potency at least comparable to that of probenecid

A single oral dose of 1 2–1 8 g of ethyl biscoumacetate is associated in man with a striking fall of serum urate levels and greatly increased urate/creatinine clearance ratios. This effect occurs 1 or 2 hours after ingestion of the drug in contrast to the longer lag required for depletion of clotting factors

The fall of the serum urate level persists during the course of daily therapy with ethyl biscoumacetate fluctuating as doses are changed, but not directly paralleling prothrombin activity The presence of considerable renal disease complicating gout does not abolish the uricosuric action of ethyl biscoumacetate

Ethyl biscoumacetate, like probenecid, enhances urate clearance in the mongrel dog In the dalmatian coach hound which has a reversed tubular transport mechanism for urate, with active secretion in addition to glomerular filtration, both drugs reduce the abnormally large urate clearance

Established uricosuric agents are known to inhibit in various degrees the tubular secretion of a group of compounds using the same transport process as active reabsorption of urate Preliminary data indicate that ethyl biscoumacetate similarly impairs the transport of P.A.H and P.S.P and may weakly affect the secretion of penicillin.

The implications of these findings are discussed. Pharmacological relationships among uricosuric anti coagulant and antirheumatic drugs are examined in the light of the newly discovered action of ethyl biscoumacetate, and the need for correlating their respective biochemical mechanisms is pointed out

Molecular structures determining participation in tubular transport are commented on and the suggestion is made that valency properties associated with tautomerism or with carbonyl unsaturation are as important in cellular reactions as a particular key substituent

Studies of related coumarin compounds may yield a useful new uricosuric agent with little or no anticoagulant activity, for the management of gout

It is interesting that urate has been implicated in coronary heart-disease the uricosuric action of ethyl biscoumacetate gives rise to speculation whether the rôle of coumarin drugs in myocardial infarction is entirely explicable by their anticoagulant effect

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REFERENCES

Berliner, R W (1954) *Ann Rev Physiol* 16 269
— Hilton, J G Yü T F, Kennedy T J jun (1950) *J clin Invest* 29 396
Beyer K H (1950) *Pharmacol Rev* 2, 227
— Russo, H F, Tillson E K, Miller A K Verwey W F Gass S R (1951) *Amer J Physiol* 166 625
Bonsnes R W Taussky, H H (1945) *J biol Chem* 158 581
Brøchner Mortensen, K (1940) *Medicine Baltimore* 19 161
Brodie, B B Weiner M, Burns J J Simson G Yale E K (1952) *J Pharmacol* 106 453
Brown, H (1945) *J biol Chem* 158 601
Byers, S O Friedman, M Garfield, M (1947) *Amer J Physiol* 150 677
Friedman, M Byers S O (1948) *J biol Chem* 175 727
Gardner J I Crisler J F jun Mircon, C J (1951) *Proc Soc exp Biol N Y* 78 460
Gertler M M, White P D (1954) Coronary Heart Disease in Young Adults Cambridge Mass
Glasgow L A J, Cookson B (1947) *Edinb med J* 54 103
— Wrigley F (1949) *Brit med J* ii 789
Gutman, A B (1951) *Bull N Y Acad Med* 27 144
— Yü T F (1951) *In* Dock W Snapper I Advances in Internal Medicine New York and London; vol V
Horwitz, M Sougin Mibashan R (1955) Paper read at Eighth International Congress of Rheumatology Geneva
— — (1955) In preparation
Hoss G W Armbruster L C A jun, Levy M D jun Wagner E J (1952) *Amer J med Sci* 223 258
Hueper W C (1946) *Arch Path* 41 592
Mason, F G W (1953) *Quart J Med* 22 331

References continued at foot of next column

DAPSONE IN DERMATITIS HERPETIFORMIS

J K MORGAN
M B Lond. M.R C P
SENIOR REGISTRAR

C W MARSDEN
M B Manc M.R C.P F
REGISTRAR

J G COBURN
B.Sc M.D Manc
CONSULTANT DERMATOLOGIST

THE MANCHESTER AND SALFORD HOSPITAL FOR SKIN DISEASES

J M MUNGAVIN
M.A M.B Camb D T.M & H.
OF THE MEDICAL DEPARTMENT, IMPERIAL CHEMICAL (PHARMACEUTICALS) LTD WILMSLOW CHESHIRE

DERMATITIS herpetiformis (Dühring's disease) is of unknown ætiology, is characterised by severe itching and grouped vesicles in the skin and persists for many years Its symptoms and signs can be suppressed by certain substances of which the most effective have hitherto been arsenic and sulphapyridine Recently sulphones have been added to the list of such agents

Dapsone (4 4′-diaminodiphenyl sulphone) was first prepared nearly fifty years ago but it was not until 1937 that its antibacterial power was reported by Buttle et al in England and by Fourneau et al in France Rist (1939) showed dapsone to be active both in vitro and in vivo against tuberculosis

Despite these observations dapsone was thought to be too toxic for use in man presumably since it could not be safely administered in the same dosage as sulphanilamide (Francis and Spinks 1950)

This toxicity led to the production of active but less toxic derivatives of dapsone (e g sulphoxone sodium and solapsone) which found a place in the chemotherapy of leprosy (Cochrane et al 1949) When it was realised that the antibacterial activity of these more complex sulphones was due to the liberation of dapsone in the body (Francis and Spinks 1950) there was a return to the use of dapsone itself in a much lower dosage Lowe (1950) had already shown that dapsone in a lower and non toxic dosage was effective in leprosy and since then dapsone has been increasingly used in leprosy

Possibly because of the antibacterial spectrum of dapsone or the apparent resemblance of its structural formula to that of sulphapyridine or its success in leprosy dermatologists began to investigate its use in certain skin diseases (Longhi 1951)

The use of sulphones in dermatitis herpetiformis was first reported by Esteves and Brandão (1950) who recorded successful control in 3 patients with di-substituted derivatives of dapsone (sulphoxone sodium 0 3–0 6 g daily and solapsone 0 5–2 0 g daily) They compared the effects of these two substances and of sulphapyridine in the same patients The patients remarked that control with the sulphones was similar to but rather less perfect than that obtained with sulphapyridine

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DR SOUGIN MIBASHAN DR HORWITZ REFERENCES—*contd*

Miller G E, Danzig L S Talbott J H (1951) *Amer J Physiol* 164 155
Overman R S, Stahmann, M A Huebner C. F Sullivan W R. Spero, L, Doherty D G Ikawa M Graf L Roseman S Link K P (1944) *J biol Chem* 153 5
Shideman F E Rene R M (1951) *Amer J Physiol* 166 104
Smith H W (1951) The Kidney: Structure and Function in Health and Disease New York.
Sougin Mibashan, R (1954) M D thesis University of Cape Town
Taggart J V (1954) *In* Wolstenholme G E W The Kidney Ciba Foundation Symposium London
Talbott J H (1943) Gout New York London and Toronto
Tulloch J A, Gilchrist A R (1951) *Amer Heart J* 42 864
Wolfson W Q, Cohn C Levine R Huddleston B (1948) *Amer J Med* 4 774
— — Shore, C (1950) *J exp Med* 92 121
Wright I S (1952) *Circulation* 5 161

Cornbleet (1951) reported the use of sulphoxone sodium in the treatment of 13 patients with dermatitis herpetiformis, over a period of up to 2½ years Some of these had previously proved refractory to other therapy, including sulphapyridine All his patients were decidedly improved, or had complete remissions, during the treatment with sulphoxone sodium A transient normocytic anæmia was the commonest side-effect The dosage was 300–900 mg daily, and Cornbleet suggested that "it was the treatment of choice in Dühring's disease "

Since the activity of the more complex sulphones depends on their hydrolysis to dapsone in the body, Kruizinga and Hamminga (1953) treated 12 cases of dermatitis herpetiformis with dapsone They reported that symptoms were controlled with doses of 100 mg daily, and concluded that the effect of dapsone in dermatitis herpetiformis was superior to that of sulphapyridine

Vickers (1954) notes that dapsone has now become the first line of defence in the control of dermatitis herpetiformis Calnan (1954) found that 29 of 30 cases of dermatitis herpetiformis treated with dapsone showed an excellent response, and he concluded that dapsone was preferable to sulphapyridine He stated that it seldom produced toxic side effects in the dosage used He recommended a dosage of 50–200 mg daily but noted that some patients could be kept well with as little as 50 mg on alternate days

After being afforded the opportunity, by Dr H R Vickers and Dr I B Sneddon, of seeing some of their cases treated with dapsone at Sheffield, we became interested in observing the effect of dapsone on patients with dermatitis herpetiformis at this hospital

Material and Method

We report here the results of treatment with dapsone over eleven months in 28 patients with dermatitis herpetiformis There were 20 males and 8 females, aged 18–72, and all had the adult form of dermatitis herpetiformis

The diagnosis was made clinically, and only patients with typical eruptions were included The majority had been under previous treatment with arsenic or sulphapyridine at this hospital for up to seven years, with varying degrees of control Several had had dermatitis herpetiformis for many years before first coming under treatment here Most of them had obtained some useful relief with either liquor arsenicalis minims 3–4 t d s by mouth or sulphapyridine 0 5–2 0 g daily These dosages had been adjusted at intervals to maintain suppression of symptoms, the intensity of which altered from time to time in accordance with the natural variations in the severity of the disease

Usually most patients had started treatment with arsenic when the condition was first diagnosed in the past After a month or so, when some suppression of the disorder was achieved, their treatment was changed to sulphapyridine In none of them had any serious toxic effects been observed with either drug, except that one patient had been unable to tolerate sulphapyridine because it provoked angioneurotic œdema As an indication of changing views on therapy, it was found that persons developing dermatitis herpetiformis in more recent years received less treatment with arsenic than did earlier patients, and latterly were given little or no arsenic at all

Dapsone was substituted for the previous therapy in the present patients primarily to determine if the eruption could be better controlled with dapsone than with previous measures, and was not done because of any toxic reactions with arsenic or sulphapyridine

The dapsone was administered by mouth in a single daily dose of 50–100 mg, varying if necessary according to the changing intensity of the eruption Full dosage was used from the outset Routine estimations of hæmoglobin were made in the early stages of therapy in nearly all cases, and in all at intervals thereafter When dapsone therapy had been used for several months, it was decided to perform also a routine series of liver function tests (comprising estimations of serum bilirubin,

TABLE I—RESULTS OF INVESTIGATION AND TREATMENT

Case no	Previous therapy			Dapsone			Toxic effects	Hæmoglobin (% Haldane)*
	Arsenic (mos)	Sulpha pyridine (yr)	Control achieved	Dose (mg daily)	Duration (mos)	Control achieved		
1	3	½	Good	100	11	Good	Nil	94- 96
2	Nil	3½	Good	50	10	Good	Nil	102- 98
3	1½	2	Poor	100–150	10	Fair	Serum bilirubin 1 6 mg per 100 ml	102- 98- 96
4	4	1½	Fair	100	10	Fair	Serum bilirubin 1 04 mg per 100 ml	118–116
5	Nil	1½	Poor	100	10	Fair	Alkaline phosphatase 15 K A units	114- 98-116
6	2	¼	Good	50–100	10	Fair	Nil	—— 98- 94
7	Intermittent	Angioneurotic œdema	Variable	50	9	Good	Nil	96- 9[illegible]- 94
8	12	Nil	Variable	50–100	9	Good	Nil	92-101-106
9	6	4	Fair	100–50	9	Good	Nil	——114
10	1½	1	Good	100	9	Good	Nil	98-104
11	1½	5	Fair	100	8	Good	Slight anæmia	94- 88- 94
12	4	3	Variable	100	7	Good	Thymol turbid 5 units serum gold +1, slight anæmia	88- 94- 94
13	2½	1½	Poor	50	7	Good	Nil	—— 98
14	Nil	Nil		50	7	Good	Nil	110-104
15	2½	5	Good	50	6	Good	Nil	90- 96- 96
16	1	4	Fair	50	6	Good	Slight anæmia	90- 84- 8
17	1½	1½	Fair	100	6	Fair	Nil	108- 96-101
18	3½	1½	Good	50–25	6	Good	Nil	90- 96
19	½	¼	Good	100	6	Good	Nil	104- 96-103
20	Nil	Nil		100	6	Good	Moderate anæmia	—— 74- 96
21	Nil	3	Poor	100	5	Good	Nil	90- 96
22	6	6	Good	50–100	5	Good	Nil	102-103
23	Nil	Intermittent	Variable	100	5	Good	Nil	98-103
24	2	Nil	Good	50	5	Good	Alk phos 25 K A units moderate anæmia, sulphæmoglobinæmia	78- 96- 50
25	Nil	¼	Fair	100–150	4	Good	Nil	106-110-106
26	3	6	Good	100–150	3	Good	Nil	96- 92
27	24	5	Good	50	3	Good	Alk phos 14 7 K-A units, slight anæmia	98- 86
28	2	2½	Good	50	3	Good	Nil	——106

* ——, Hb not estimated

alkaline phosphatase, and plasma protein and the empirical liver function tests—thymol turbidity, thymol flocculation, and serum gold tests) on any patients who had received dapsone for more than two months. All the patients in this series had one such test This was introduced because hepatitis had been reported as a toxic side-effect (e.g Cochrane et al. 1949 Molesworth and Narayanaswami 1952) although Smith (1950) considered that dapsone could not be shown to have any effect on the liver function in a dosage of less than 300 mg daily

All the patients in this series received treatment with dapsone for at least three months The control adopted was that available through the nature of the disease itself which promptly relapsed if the suppressive treatment was omitted or if the dosage of dapsone became inadequate The comparison with any previous therapy was retrospective and based on a clinical appreciation of the condition of each patient This was usually substantiated by the patient's subjective impressions.

In the assessment of the degree of response the following arbitrary standards were selected both for dapsone and for the previous suppressive therapy

Good complete suppression of signs, or with only occasional excoriations, crusted papules or blisters. No itching.

Fair a few lesions most of the time but never severe Some itching

Poor many lesions and much itching

Variable suppression varied between fair and poor" Usually applied to patients who had only taken their suppressive drug irregularly or intermittently

Results

The results of treatment together with the results of routine investigations are shown in table I

Biochemical Investigations

Cochrane et al. (1949) suggested that the skin might have a selective ability to fix dapsone but Smith (1949) Dharmendra et al (1950) Lowe and Davey (1951) and Francis (1953) did not support the hypothesis Nevertheless some workers still felt that selective concentration of dapsone in the skin might take place and could therefore explain the action of dapsone in leprosy and in dermatitis herpetiformis

We therefore felt that an investigation of the levels of dapsone in the blood and skin of some of our patients would be useful, because it might explain the action of dapsone in dermatitis herpetiformis and because of the interest of leprologists in these levels

Samples of blood were taken from 6 patients and paper specimens of skin from 4 patients The method used for determination of free dapsone in the blood was that described by Francis and Spinks (1950)—namely extraction from disodium hydrogen phosphate buffered blood into benzene, transfer into hydrochloric acid followed by diazotisation and coupling to N-β-sulphato ethyl m toluidine Local anæsthetics containing a primary aromatic amino group (e g procaine) interfere with this method because they take part in the diazotisation thus giving rise to figures for dapsone which are much higher than they should be We therefore did the skin biopsies under trichloroethylene analgesia with the Cyprane inhaler before determining the amount of free dapsone in the skin by the same method as described for blood.

Because of the low skin-dapsone level in case 3 it was decided to pool the skin samples from the remainder (cases 4 10 and 15) taking the mean value because this would facilitate the estimation of the very small quantity of dapsone available in the biopsy material

TABLE II—LEVELS OF DAPSONE IN BLOOD AND SKIN

Case no	Blood dapsone (mg per 100 ml)	Skin dapsone (mg per 100 g)	Dosage of dapsone at time of biopsy
3	0·34	0·01	100 mg daily for last 29 wk.
4	0·21	0·13	100 mg daily for last 8 wk.
10	0·27	0·13*	100 mg daily for last 21 wk
15	0·09	0·13	50 mg daily for last 10 wk.
8	0·17	No biopsy	50 mg daily for last 12 wk.
18	0·12	No biopsy	50 mg daily for last 3 wk

Skin samples from cases 4 10 and 15 were pooled

The levels of dapsone found in blood and skin are recorded in table II which shows that there was no selective concentration of dapsone in the skin compared with the blood Since our observations agree with those of Smith (1949) Dharmendra et al (1950) and Lowe and Davey (1951) in man and Francis in animals (1953), we suggest that all the available evidence is against the hypothesis that dapsone is specifically accumulated in the skin

Discussion

Dermatitis herpetiformis is much subject to periodical variation in intensity and tends in some cases to become less severe with the passage of many years For this reason a long period of study is required to establish the true worth of a new therapeutic agent However our early results have been encouraging In 23 of our 28 patients (82%) there was very good control of their eruptions In the remaining 5 (18%) a fair degree of control was achieved

A comparison of the efficacy of dapsone and that of sulphapyridine was possible in retrospect, in 23 patients 8 of these (35%) were very much better when receiving dapsone than they had been with sulphapyridine and a further 2 (9%) had a somewhat greater degree of suppression of symptoms with the newer treatment 12 patients (52%) had an approximately equal degree of control with either drug 1 patient (4%) had obtained better results with sulphapyridine in his case the suppression was 'good' with sulphapyridine but only fair with dapsone

In 5 of the patients no comparison between dapsone and sulphapyridine was possible 4 of them had never received sulphapyridine and 1 had been unable to tolerate it because it provoked angioneurotic œdema Of these patients 3 had received arsenic for short periods The remaining 2 patients had been treated with dapsone from the time of their first attendance

Many patients volunteered that they preferred dapsone to sulphapyridine and found the itching suppressed more rapidly by dapsone However it must be noted that, while receiving dapsone patients may have been kept under a more intense regular and critical scrutiny than they had received previously and dosage levels were perhaps adjusted with greater promptitude as the disease fluctuated

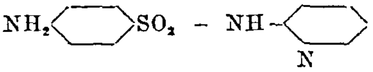
The highest dosage used was 150 mg daily and most patients found 50–100 mg daily sufficient None began treatment with less than 50 mg a day No attempt was made to induce treatment slowly with small initial doses and a gradual subsequent increase to a therapeutic level in the manner recommended by Lowe (1950) However Lowe was using daily doses which were *ultimately* much larger than those used by us

Up to now no serious toxic effects have been observed from dapsone Some anæmia as described by previous workers was observed in 6 cases in the early stages of therapy but was not troublesome and never became an indication for stopping the treatment. In all those in whom the measure was deemed necessary the anæmia responded to iron by mouth 2 patients showed cyanosis in case 24 spectroscopy of the blood showed the absorption band of sulphæmoglobin (though not of methæmoglobin), and in case 6 the cyanosis was cardiovascular in origin and related to auricular fibrillation and hypertension There were no instances of jaundice, and on the basis of liver-function tests we did not obtain evidence of gross liver dysfunction in any patient 2 patients (cases 3 and 4) had moderately raised serum-bilirubin levels, and case 12 showed slight abnormalities in the empirical tests In addition 3 patients (cases 5, 24, and 27) had raised blood-alkaline phosphatase levels No single patient showed any combination of these abnormalities, and usually the departure from normal values was slight The total number of cases in our series is not large, and it may not be wise at this stage to dogmatise on the question of liver damage from administration of dapsone for dermatitis herpetiformis Liver-function tests of the type we applied do not exclude minor degrees of hepatic dysfunction Lowe (1951) has commented that the occurrence of liver damage in patients receiving dapsone may have been related to the fact that they were already suffering from nutritional deficiencies In many cases where jaundice was reported dapsone was being administered in much larger dosage than in our patients However, Howell (1955) reports a possible instance of toxic hepatitis in a woman who had been given dapsone 50 mg daily for dermatitis herpetiformis None of our patients developed a drug eruption or a psychosis while taking dapsone

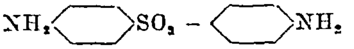
This absence of serious toxic effects in our series, coupled with the initial full dosage, was one reason why it was suggested to us that dapsone might be selectively concentrated in the skin in dermatitis herpetiformis The result of investigation on this point in 4 of the present patients does not support this hypothesis There was no selective concentration of dapsone in the skin compared with blood-dapsone levels

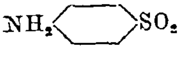
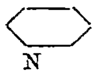
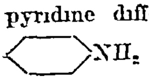
The good response of patients with dermatitis herpetiformis to dapsone does not so far appear to help towards elucidating the ætiology of the disease Dapsone and sulphapyridine are both merely suppressive agents, and dermatitis herpetiformis relapses rapidly if the treatment is omitted Possibly the apparent likeness between the structural formulæ of dapsone and sulphapyridine may have led earlier workers to use dapsone in dermatitis herpetiformis, which they knew was favourably influenced by sulphapyridine Calnan (1954) has called attention to the similarity of the structural formulæ

Sulphapyridine



Dapsone



It is, of course, possible that the common feature  may have something to do with their action in dermatitis herpetiformis, just as presumably it has in relation to their antibacterial action However, from the chemical standpoint the linkage →C—SO_2—C← of dapsone is very different from the linkage →C—SO_2—NH of sulphapyridine Moreover the chemical properties of the pyridine ring  in sulphapyridine differ radically from those of the grouping  *in dapsone*

The facts that sulphapyridine is the only sulphonamide known to be effective in Dühring's disease, and that this property is shared with dapsone, seem to constitute just one of the many problems of chemotherapy which we ca [illegible] lain, for in our view any resemblance between their structural formulæ is "pictorial" rather tha constitutional.

Conclusions

The degree of suppression of the signs and symptom of dermatitis herpetiformis with dapsone is good and, i this series, tended to be more satisfactory than wit previous therapy

Our experience confirms the impressions of others tha dapsone is the drug of choice in dermatitis herpetiformis Nevertheless 1 patient seemed to obtain better relief with sulphapyridine, and 12 patients had an equal degree of control with either drug For this reason we suggest that sulphapyridine should not be discarded entirely at present

The rapid effectiveness of dapsone in dermatitis herpeti formis and the absence of serious toxic reactions with the dosage used are not explained by any selective concentration of dapsone in the skin

Summary

The results of treating 28 cases of dermatitis herpeti formis with dapsone for three to eleven months are reported

With a daily dosage of 50–150 mg good control of the disease was achieved in 23 patients (82%), and fair control in the remaining 5 (18%)

Comparison with previously administered sulpha pyridine suggested that dapsone was usually the more effective

No serious toxic effects were observed Some anæmia developed early in the treatment in several cases, but there was no evidence of either jaundice or gross liver dysfunction Minor abnormalities were indicated by liver function tests in 6 patients 1 patient developed sulphæmoglobinæmia

A biochemical study in 4 patients with dermatitis herpetiformis showed no selective concentration of dapsone in the skin

Though dapsone now appears to be the drug of choice in dermatitis herpetiformis, sulphapyridine is of equal value in many cases and may be the more effective therapy in a few

The similarity in chemical configuration between sulphapyridine and dapsone is more apparent than real. We feel that this superficial likeness does not explain their comparable ability to control dermatitis herpeti formis

Our thanks are due to the consultants of the Manchester and Salford Hospital for Skin Diseases for permitting us to study and treat the patients under their care, to Dr R G Cochrane, who suggested the biochemical investigations, to Dr R R Goodall, of the I C.I Research Department, who carried them out, and to the patients for their coöperation

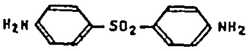
REFERENCES

Buttle, G A H, Stephenson D Smith, S Dewing, T Foster G E (1937) *Lancet*, i, 1331
Calnan, C D (1954) *Trans St John's Hosp derm Soc, Lond* 33, 53
Cochrane R. G Ramanujam, K, Paul, H Russell, D (194 *Leprosy Rev* 20, 4
Cornbleet T (1951) *Arch Derm Syph, Chicago* 64, 684
Dharmendra, Chatterjee K. R, Bose R (1950) *Leprosy in Ind* 22, 174
Esteves J Brandão F N (1950) *Trab Soc portug Derm.* 8
Fourneau E Tréfouël J Nitti, F Bovet, D, Tréfouël J (193 *C R Acad Sci Paris*, 204 1763
Francis J (1953) *J comp Path* 63 1
— Spinks, A (1950) *Brit J Pharmacol* 5 565
Howell R G (1955) *Brit med J* i 542
Kruizinga E E Hamminga H (1953) *Dermatologica, Basel*, 106
Longhi A (1951) *Rif med* 65, 345
Lowe, J (1950) *Lancet* i, 145
— (1951) *Ibid* i 18
— Davey T F (1951) *Trans R Soc trop Med Hyg* 44
Molesworth B D Narayanaswami P S (1952) *Lancet* i
Rist N (1939) *C R Soc Biol Paris* 130, 972
Smith M (1949) *Leprosy Rev* 20, 78
— (1950) *Ibid* 21, 17
Vickers, H R (1954) *Practitioner*, 173 373

DAPSONE IN THE TREATMENT OF DERMATITIS HERPETIFORMIS

J O'D ALEXANDER
M.B Birm. F.R.F.P.S
THIRD ASSISTANT PHYSICIAN DEPARTMENT OF DERMATOLOGY, GLASGOW ROYAL INFIRMARY

Cornbleet (1951) reported encouraging results in the treatment of 12 cases of dermatitis herpetiformis with Diasone' This substance like Promin and Sulphetrone (solapsone) is a substitution product of 4 4 diaminodiphenyl sulphone (dapsone *B.P C*) which has the following structural formula



These substitution products originally introduced because of their supposed therapeutic superiority over the parent substance and because they were thought to be less toxic in fact owe their therapeutic activity to the liberation and absorption of dapsone

Kruizinga and Hamminga (1953) have reported excellent response to dapsone in 12 cases of dermatitis herpetiformis I report here the effects of dapsone in 28 cases

The disease is manifested by an eruption of grouped urticarial papules vesicles bullæ or even pustules which tend to have a characteristic distribution The lesions are commonly found around the elbows over the scapular areas, on the outer sides of the hips across the sacrococcygeal region and around the front of the knees More than one variety of lesion may be present The lesions recur continuously in the same area and are intolerably itchy In most cases dapsone causes complete suppression of itching in a day or two and the lesions clear up within a week Continuation of treatment prevents recurrence Kruizinga and Hamminga (1953) have made it clear, however, that dapsone only suppresses the disease; it does not cure Withdrawal of dapsone leads to prompt relapse The itch usually returns within forty-eight hours and is rapidly followed by a fresh eruption of lesions, which in their early stages tend to be monomorphic—i.e all urticarial all vesicular or all bullous The herpetiform appearance is more often appreciated during a relapse than in the chronic untreated case

Method of Administration

Dapsone is given by mouth According to Smith (1950) the largest tolerated dose, as used in leprosy, is 300 mg daily In the present series the initial dosage was arbitrarily fixed at 200 mg daily for the first week, followed by 100 mg daily for the next two weeks Thereafter the dosage was adjusted to the minimum required to suppress symptoms If the initial dosage was inadequate it was increased to 300 mg daily for a maximum of two weeks and then gradually lowered to the minimal maintenance dose If 300 mg daily did not control the dermatitis, treatment with dapsone was stopped

Results

Of the 28 patients 19 were males The 28 patients were aged 10–86 19 of them being between the ages of 20 and 60 A widespread generalised and often polymorphic rash with much evidence of excoriation was classed as severe there were 6 such cases A moderately severe case was one in which there was an abundance of lesions confined to certain areas of predilection there were 16 such cases The remaining 6 cases were mild with only few lesions in one or more of the characteristic sites

24 cases were successfully controlled and observed for periods varying from nineteen to seventy-one weeks In 4 cases the treatment was stopped without causing an immediate relapse 3 of them have remained clear for fourteen sixteen and thirty four weeks and the 4th relapsed after six weeks, and treatment had to be restarted Treatment was stopped in 2 other cases 1 had a sudden unexplained rise in blood urea level, and the other, aged 86 had a persistent reticulocytosis (10%) In neither case was the treatment recommenced The maintenance doses were

—	< 100 mg daily	100 mg daily	> 100 mg daily
Severe	2	1 (1 remission)	0
Moderate	3	10 (1)	2
Mild	3 (1 remission)	1	2 (1 remission)
Total	8	12	4

The maintenance dose in most cases was 100 mg daily or less, regardless of the severity

Treatment was deliberately withdrawn in 4 cases for a week In several others treatment was inadvertently stopped by the patients for a few days at a time, for reasons such as shortage of supply In every case there was an immediate relapse, which was easily controlled by resumption of therapy as for untreated cases 12 of the cases had previously been treated experimentally with various sulphonamides other than sulphapyridine and with placebos (lactose tablets) All of these cases relapsed under such treatment

Of the 4 cases unsuccessfully treated with dapsone, 3 were severe Partial control was achieved in 1 of these but the maintenance dose required for even this effect was 300 mg daily, and it was felt that this was too large for long continued administration Neither of the 2 other cases nor 1 moderately severe case showed any favourable response to dapsone

Toxic Effects

Benson and Goodman (1945) listed the toxic effects of diasone (which are similar to those of dapsone) The commonest *subjective effects* were fatigue nervousness vertigo headache, and dyspnœa and anorexia, nausea epigastric distress diarrhœa disorientation restlessness insomnia, tremors, *diplopia myalgia* and palpitation also occurred Other workers agree with this list (Pfuetze and Pyle 1945, Floch and Destombes 1949, Cochrane et al 1949, Rist and Cottet 1949) Pfuetze and Pyle add that these symptoms are often aggravated pre existing complaints. Among the objective effects only cyanosis and anæmia are common but agranulocytosis, [illegible] *dermatitis jaundice tachycardia fever*, and enlargement of the thyroid gland have also been reported

In the present series subjective effects were trivial and included dyspnœa (3), tiredness (3), headache ([illegible]) nausea (2) anorexia (1), and palpitation (1)

18 patients were clinically cyanosed (7 severely) Only 2 patients showed a temporary decrease of hæmoglobin of more than 10%, the greatest being 21% In [illegible] patient the blood urea level rose temporarily to 150 [illegible] per 100 ml., it began to fall before the dapsone was withheld The only evidence of liver dysfunction was a temporary increase of thymol turbidity in [illegible] other liver function tests including examination for urobilin were negative (Ehrlich's aldehyde [illegible] urobilinogen is invalidated by dapsone) White [illegible] the leucocyte count was constantly within

Discussion

Dapsone is a potent therapeutic weapon [illegible] of dermatitis herpetiformis It rapidly [illegible] and symptoms and a small maintenance [illegible] keep them in abeyance In this [illegible] sulphapyridine and it is just as [illegible] experience no case which has [illegible] has failed to respond equally [illegible] being smaller, are easier to [illegible] experienced both are in [illegible] dapsone It does not [illegible] depression often caused

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drugs are similar also in that neither cures the disease, and withdrawal of therapy usually leads to relapse With both, the maintenance dose may be extremely small one of my patients was controlled with 0 25 g of sulphapyridine daily, and 2 of the present cases needed only 100 mg of dapsone once weekly

Lowe (1952), discussing the use of dapsone in the treatment of leprosy, said that slow induction of treatment with dapsone minimised the risk of acute toxic effects Kruizinga and Hamminga (1953), in accordance with this dictum, advocated an initial dose of 50 mg daily, to be gradually increased until control was achieved The dose was then lowered slowly until the minimum maintenance level for the individual case was reached The method used in the present series, in which I started with a moderately high dose, was devised by analogy with the dosage used in treatment with sulphapyridine My experience with sulphapyridine suggested that an initial inadequate dose often caused difficulty in controlling dermatitis herpetiformis, whereas a short period of initial high dosage rapidly controls the disorder Dosage may then be quickly reduced to the required maintenance level This method seems to work just as well with dapsone Apart from cyanosis, the toxic effects seen were few and very mild and transient This bears out the generally accepted view that patients develop a tolerance to sulphones—a tolerance that does not affect the therapeutic efficacy of the drug but only its toxic effects (Rist and Cottet 1949) Cyanosis must be excepted from this statement

Cyanosis—Several workers are agreed that the degree of cyanosis bears no constant relation to the blood-level of dapsone (Pfuetze and Pyle 1945, Benson and Goodman 1945) This appeared to be true of the 17 patients developing cyanosis in this series There was no correlation between the degree of cyanosis and the dosage of dapsone Unlike other side effects, cyanosis seems to persist indefinitely but is not associated with any subjective phenomena The cause of the cyanosis is undoubtedly the presence of methæmoglobinæmia This has been confirmed in many cases by Dr A G Baikie

Although there was little anæmia in any case, there was evidence of mild hæmolysis in several In 1 case the hæmoglobin was reduced by 24% but was restored without stopping treatment

Control of Treatment—Muir (1950), discussing the control of treatment of leprosy with dapsone, says that "hæmoglobin estimation together with clinical signs and symptoms is a safe guide to the amount of dapsone tolerated" In the present series many other investigations were also made, but the fifteen months' experience of treating dermatitis herpetiformis with dapsone confirms Muir's statement

Summary

The use of dapsone *B.P C* in the treatment of dermatitis herpetiformis is described

28 cases were treated, with excellent control in 24

The toxic effects of the drug are discussed, and requirements for control of treatment are determined

The relative merits of dapsone and sulphapyridine are compared

I wish to thank Dr G Harvey for permission to publish these cases, and Dr Baikie for investigating the hæmatological effects of dapsone

REFERENCES

Benson L, Goodman, L (1945) *Amer Rev Tuberc* 51 463
Cochrane, R G, Ramanujam K, Paul, H., Russell, D (1949) *Leprosy Rev* 20, 4
Cornbleet, T (1951) *Arch Derm Syph, Chicago*, 64 684
Floch H, Destombes P (1949) *Int J Leprosy* 17 367
Kruizinga E. E Hamminga H (1953) *Dermatologica, Basel* 106, 387
Lowe J (1952) *Leprosy Rev* 23 4
Muir E (1950) *Int J Leprosy*, 18 299
Pfuetze, K H Pyle M. (1945) *Dis Chest*, 11, 213
Rist, N Cottet, J (1949) *Pr méd* 57 743
[illegible] 1950) *Leprosy Rev* 21, 17

CHEMICAL SKIN SEX IN "OVARIAN" AGENESIS

P E POLANI
M D Pisa, M R C P, D C H.
LATE ASSISTANT TO THE DIRECTOR, DEPARTMENT OF CHILD HEALTH

I A MAGNUS
B A, M.B Camb, M.R C P
REGISTRAR AND RESEARCH FELLOW, SKIN DEPARTMENT
GUY'S HOSPITAL, LONDON

THE name of Turner is associated with the syndrome of dwarfism, webbed neck, valgus deformity of the elbow, and sexual infantilism, though its various components had been recognised by previous workers The syndrome manifests itself almost only in females, but cases of webbed neck and dwarfism have been reported also in males Wilkins and Fleischmann (1944), on the grounds of original observations and previously published cases, showed that the gonads of the female patients were devoid of primordial follicles, and named the syndrome "ovarian agenesis" Similar ovarian maldevelopment has also been seen in patients without the gross malformations described by Turner, of course, sexual infantilism is always present, and dwarfism nearly always. Males with webbed neck and dwarfism always have testicles, though generally they are not quite normal.

By chromosomal sexing of skin (Moore et al 1953) it was shown that the pattern of sex chromatin in females with Turner's syndrome corresponds to that of normal males, and it was therefore suggested that these patients may in fact be genetic males with gonadal maldevelopment and intra-uterine feminisation (Polani et al 1954) The results of independent work done by Wilkins et al (1954) and their conclusions support this finding

Pseudocholinesterase Content

Magnus and Thompson (1954) studied the esterase content of normal skin by essaying manometrically the hydrolytic activity of specific enzymes on individual substrates Thus they showed that biopsy specimens of skin taken from males contain significantly smaller amounts of pseudocholinesterase than do those taken from females, the reason for this was unknown

To clarify the significance of this finding in relation to the absence of gonads, and to obtain further data on the sex of patients with "ovarian agenesis," we estimated the pseudocholinesterase content of the axillary skin of nin patients whose biopsy specimens of skin showed a m[illegible] pattern of sex chromatin (see table) and whose leucocyte whenever examined, showed the same pattern (Davidso and Smith 1954) The diagnosis was made on clinic grounds without gonadal biopsy and was supported by

ANALYSIS OF CASES

Age (yr)	Apparent sex	Diagnosis	Chromosomal sex		Pseudocholinesterase activity (µl of CO_2 per g per hr)
			Skin	Leucocytes	
12	F	T S	M	M	2083
13	F	O.A	M	M	1395
14	F	O A	M	M	1798
18	F	T S	M	M	161*
18	F	T S	M		1710
20	F	T.S	M	M	1256
22	F	O.A	M	M	963
23	F	O A	M	M	1203
27	F	O A	M		1069

T S Turner's syndrome
O A "ovarian agenesis"—i e dwarfism and minor stigmata but without the grosser malformations described by Turner
Mean value for axillary skin of the patients 1431 ± 110
Mean value for axillary skin of normal males 626 ± 40
Mean value for axillary skin of normal females 1326 ± 114
Mean value for other skin areas of normal males 770 ± 3
Mean value for other skin areas of normal females 1148 ± 34

laboratory findings All values of pseudocholinesterase except one borderline, fell within the normal range for women. The mean of the values was not significantly higher than the mean for normal skin in the area of biopsy

Conclusions

If it be accepted that chromosomal sexing detects the genetic sex of the individual, one can state that the pseudo-cholinesterase content of the skin of these patients was not related to their genetic sex but accorded with their apparent sex Because one measures the enzyme content in a unit of weight of skin differences in skin thickness will cause different amounts of enzyme to be assayed. Therefore possibly the pseudocholinesterase content of the skin of our patients was related only to its thickness which thus would be similar to that of normal females Alternatively, the level of skin pseudocholinesterase *may reflect actual differences in concentration* due to nutritional or metabolic states (Waterlow 1950 Magnus and Thompson 1954) in which case it may be influenced by hormonal balance

We are indebted to Dr P M F Bishop and Dr P R Evans and to Prof F T G Prunty for access to the cases under their care Dr Bernard Lennox for sexing the biopsy specimens of skin and Prof R H S Thompson for his interest and suggestions.

REFERENCES

Davidson, W. M, Smith, D R. (1954) *Brit med J* ii 6
Magnus, I A., Thompson, R. H S (1954) *Brit. J Derm.* 66 103
Moore, K. L. Graham M. A Barr M. L. (1953) *Surg Gynec Obstet.* 96 641
Polani, P E Hunter, W F, Lennox, B (1954) *Lancet* ii 120
Waterlow, J (1950) *Ibid* i 908
Wilkins, L. Fleischmann, W (1944) *J clin Endocrin* 4 357
— Grumbach, M. M., Van Wyk, J J (1954) *Ibid* 14 1270

CRIPPLING DYSPNŒA WITH HEALING

A DANGER OF EFFECTIVE CHEMOTHERAPY IN PULMONARY TUBERCULOSIS

S E Slade
M.B Lond
MEDICAL REGISTRAR, WINDSOR CHEST CLINIC BERKS

Since the introduction of effective chemotherapy in the treatment of pulmonary tuberculosis many undesirable side effects have been described (Riches 1954 Dixon 1954 Hughes et al 1954)

My present object is to show that treatment which cures may constitute a greater danger to the patient than the disease from which he has been delivered Three representative cases are reported The first ended fatally the second patient *is a* pulmonary cripple; and the third has made a useful recovery

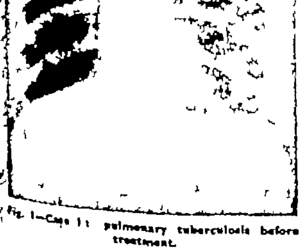

Fig. 1—Case 1: pulmonary tuberculosis before treatment.

Case reports

Case 1 —A woman aged 27 had been diagnosed as having pulmonary tuberculosis nine years previously when she was shown to have widespread disease of the right lung and extension into the left upper zone (fig 1) Sanatorium régime was instituted with a pneumoperitoneum a right phrenic crush, and a left artificial pneumothorax Her sputum remained positive and a right $6^1/_2$ rib thoracoplasty was done three years later The left artificial pneumothorax was abandoned after five years. In September 1954 she was *living at home* cared for by her mother She could manage the stairs between the ground floor and her bedroom unaided but with difficulty Her cough was troublesome and interfered with sleep and she produced 4–6 oz. of sputum daily containing acid fast bacilli. Chest radiography revealed the condition shown in fig 2 Treatment was continued at home with streptomycin isoniazid and *p* aminosalicylic acid After twelve weeks treatment the patient reported that her cough was no longer troublesome her sleep was unbroken for the first time for years, and her sputum *amounted to only* a thimbleful each day In spite of this relief of symptoms she began to be increasingly breathless during the next three weeks even movement in bed distressed her At this stage she had nausea although without much vomiting and all chemotherapy was stopped for this reason but retching continued to exhaust her

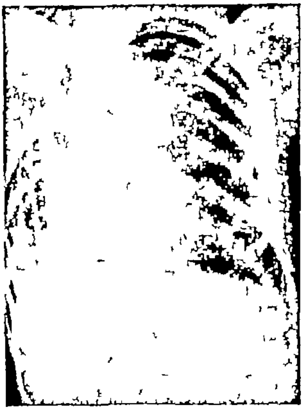

Fig. 2—Case 1: condition of lungs after five years treatment by pneumoperitoneum right phrenic crush left artificial pneumothorax, and right thoracoplasty

On examination she was mildly confused, and there was central cyanosis Speech was difficult because of dyspnœa. She was not anæmic, and there was no deterioration of the physical signs in the chest Her pulse was rapid and thready, there was no peripheral œdema although her neck veins were filled and the liver was palpable but painless Response to digoxin was transitory and she died from pulmonary insufficiency four days later There was no necropsy

Case 2 —A man aged 53 with twenty four years history of pulmonary tuberculosis with positive sputum developed in April 1953 a submucous rectal abscess which discharged through a short direct fistula a year later This was laid open by Mr W B Gabriel in June 1954 Previous treatment had been restricted to sanatorium régime and six weeks treatment with strepto-

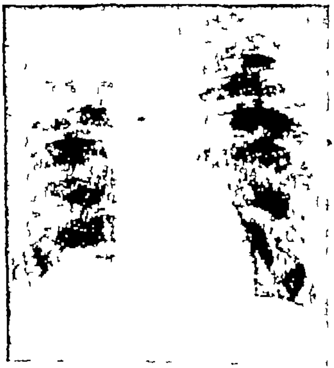

Fig 3—Case 2: condition of lungs after twenty-four years pulmonary tuberculosis.

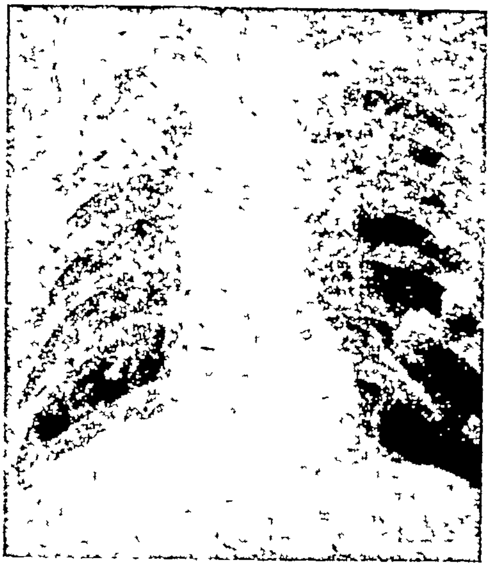

Fig 4—Case 3: condition of lungs after two years' pulmonary tuberculosis

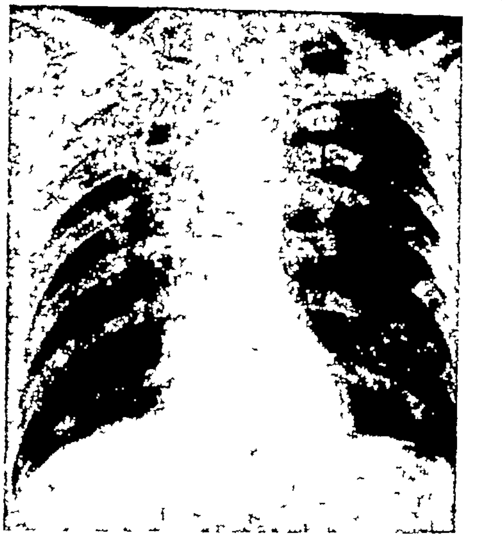

Fig 5—Case 3 condition of lungs after twelve weeks' treatment with streptomycin and isoniazid

mycin and isoniazid Chest radiography revealed the condition shown in fig 3 In September, 1954, tubercle bacilli grown from his sputum were insensitive to streptomycin, and he was given *p* aminosalicylic acid and isoniazid for a year At that time the patient could walk slowly to the village and help his wife in the garden Four weeks after starting treatment he was so short of breath that he could not move about the house unaided He has remained so ever since, although his fistula has healed

Case 3—A male groom, aged 65, first seen in September, 1953, *had two years' history of productive cough, increasing* lassitude, and interrupted sleep He was found to have bilateral excavating disease of the lungs (fig 4) His erythrocyte sedimentation rate (E.S.R.) was 57 mm in 1 hr (Westergren) and his sputum contained tubercle bacilli He could manage the 52 steps up to his living quarters with difficulty

Treatment with streptomycin and isoniazid was started at home Eight weeks later he felt much better, was sleeping well, and managed the stairs as before Radiological improvement was insignificant, the E.S.R. was 32 mm in 1 hr, and the sputum still contained tubercle bacilli Over the next four weeks the patient became cyanosed, very short of breath, and unable to move about his room without help, although his cough no longer troubled him Radiography showed improvement in the lungs (fig 5), and culture of his sputum was negative for tubercle bacilli although a few acid fast structures had been seen on direct smear Treatment was continued, and a month later his symptoms had subsided sufficiently to enable him to manage the stairs once more Since then his chemotherapy has continued to a total of fourteen months, and he has now resumed most of his activities (fig 6) His sputum remains negative for tubercle bacilli.

Discussion

Chronic tuberculosis of the lungs is a host parasite relationship in which the slow process of fibrosis is often compatible with many years of life, during which the persistence of *Mycobacterium tuberculosis* in the diseased tissue delays healing and continues to stimulate the formation of new granulations (Cappell 1951) The abrupt removal of this stimulus by effective chemotherapy may accelerate fibrosis of the diseased tissue (Dick 1954) When the [illegible] is sufficiently widespread, this relatively [illegible], although accompanied by arrest of necrosis, disturbs the remaining lung parenchyma in such a way as to impair pulmonary function The pathology is not clear but seems likely to be compensatory vesicular emphysema of the residual lung tissue

To distinguish patients who will benefit by medical treatment from those who will deteriorate is difficult, simple pulmonary-function tests applied before treatment are unsatisfactory guides because they do not indicate the pulmonary reserve likely to remain when the tuberculosis has been cured

The present three cases suggest that the use of effective antituberculous chemotherapy in widespread chronic tuberculosis may be more harmful than the natural course of the illness

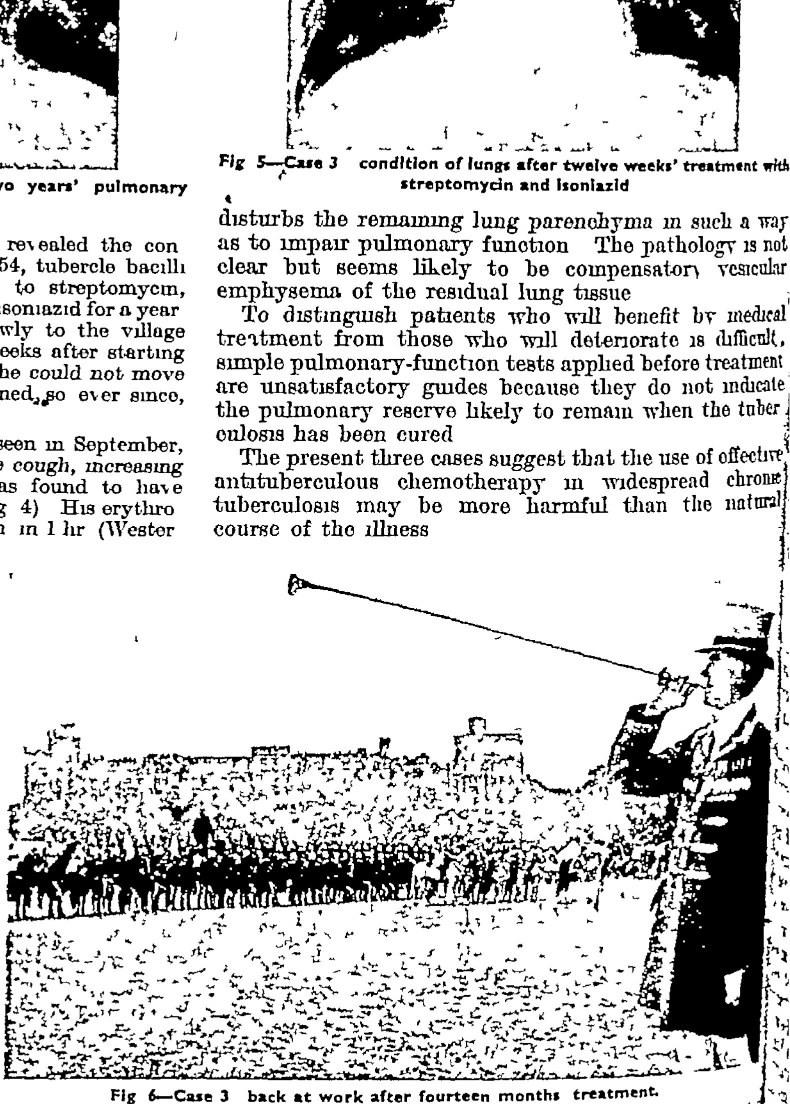

Fig 6—Case 3 back at work after fourteen months treatment.

I wish to thank Dr B C Thompson for permission to publish these cases observed at the Windsor Chest Clinic, Dr E J Holborow for his helpful criticism, and Miss D. Bannister for preparing the illustrations

REFERENCES

Cappell, D F (1951) Muir's Text Book of Pathology Lond pp 84 and 86
Dick, J C (1954) *Lancet* ii 516
Dixon, W M (1954) *Brit J Tuberc* 48, 102
Hughes, H B Biehl, J P, Jones, A P, Schmidt, L H *Amer Rev Tuberc* 70, 266
Riches, H R C (1954) *Brit J Tuberc* 48, 298

Medical Societies

ROYAL SOCIETY OF MEDICINE

Juvenile Rheumatism

On May 25 the section of pædiatrics met under the chairmanship of Mr G H MACNAB, its president to discuss Juvenile Rheumatism

Dr BERNARD SCHLESINGER said that thirty years ago every tenth bed at Great Ormond Street was occupied by a child with rheumatic fever now it was difficult to find even enough cases to conduct controlled trials of the newer methods of treatment Medical examinations in L.C.C schools revealed a similar decline in the incidence of rheumatic heart disease over a period of decades In 1947 notification of acute rheumatic fever had been introduced in some regions and in the last seven years such notifications had maintained a steady rate of 0 5–0 3 cases per 1000 population The cause of this decline was no doubt associated with the diminishing incidence of group A streptococcal infections Glover's figures for the parallel fall over eight decades in the death rate from scarlet fever another group A streptococcal disease were very striking Dr Schlesinger recalled how severe some of the acute cases were even twenty or thirty years ago, when heart failure and death were much commoner; but the incidence of chorea had decreased much less There could be no complacency over the present mildness and rarity of the condition Cyclical changes in disease pattern were a commonplace of epidemiology and Dr Schlesinger emphasised that present trends in the natural history of rheumatic fever began long before the introduction of effective antibiotic prophylaxis of streptococcal infections. The change in age distribution was also very remarkable In the '80s the mortality was greatest in the middle aged and elderly, and the disease was primarily one of adults Now the pattern was completely reversed Speaking of ætiology Dr Schlesinger underlined the lack of advance in this field since Dr W R F Collis in Eire and Dr A F Coburn in America had drawn attention to the association with group A streptococcal infections Results of present research in England were interesting and even promising but there was clearly a long way to go before any alternative or adjunct to antistreptococcal prophylaxis was produced

Dr E G L BYWATERS described a joint American and British attempt to assess (*a*) the relative effectiveness of corticotrophin cortisone and aspirin in modifying the course of the acute attack, and (*b*) the relative effectiveness of these three agents in suppressing subsequent heart-disease This clinical experiment was carried out at six centres in Britain and six in the U S.A. Altogether 500 cases, divided into three treatment groups were available for comparison during treatment and follow up The rigid diagnostic criteria for inclusion of cases in the trial and the strictly random allocation of cases to each treatment group resulted in close homogeneity of treatment groups Treatment was given for six weeks The somewhat disappointing conclusions which had so far emerged were (*a*) that on any of the three treatments some fresh manifestations of acute rheumatism developed in some cases although hormones were a little more effective in suppressing the acute attack; (*b*) that rebound phenomena were common after cessation of treatment (*c*) that nodules disappeared more quickly on hormone treatment and (*d*) that there was no difference in heart status between the treatment groups at the present stage of follow up

Dr GERALD THOMAS spoke of the early diagnosis of heart involvement in acute rheumatic fever In his experience the so-called classical signs were often wanting thus tachycardia was unusual except in severe case while cardiac enlargement was rare in the early stage The radiographic appearances of dilatation were due more often to pericardial effusion and he showed radiographs illustrating how effusions occurring early in the acute attack may clear up within a few weeks without residual heart damage Pericarditis occurred in only 15% of cases in the special unit for juvenile rheumatism at Taplow Electrocardiographic abnormalities (prolonged P–R interval, QTC) were found in only a quarter of the cases The significance of soft basal and apical diastolic murmurs and of mitral systolic murmurs had been clarified by follow up studies at Taplow Where loud murmurs were present on admission or developed after admission, follow up usually showed residual cardiac damage Where no clinical or radiographic evidence of carditis was found in the acute attack no cardiac damage was found at follow up In cases where there was minimal evidence of carditis the nature of the murmur was of prognostic significance Dr Thomas drew attention to soft diastolic murmurs developing soon after admission When these were transitory, it was unusual to find evidence of cardiac damage at follow up after three years When these soft diastolic murmurs were constant evidence of cardiac involvement—usually a basal diastolic murmur—was commonly found at follow up Dr Thomas did not think therefore that the transitory mitral diastolic, or Carey Coombs murmur is a precursor of mitral stenosis but rather that a basal diastolic murmur constantly heard is a sensitive index of slight residual heart damage

Dr W R F COLLIS (Dublin) recalled the experiences which had led him twenty five years ago to the view that group A streptococcal infections were ætiologically related to rheumatic fever He was convinced that an antibody antigen reaction was responsible for the rheumatic lesion and on this he based treatment—penicillin to eradicate the infecting organism and cortisone to modify the antibody response and the reaction of the body to its consequences

In reply to questions Dr SCHLESINGER observed that the incidence of rheumatic fever had ceased to drop in 1946 and was now running at a steady low level With regard to prophylaxis he favoured oral penicillin as the safest and most effective agent for preventing streptococcal infections in rheumatic subjects

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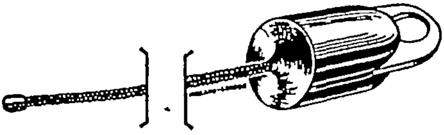
New Inventions

A VARICOSE-VEIN STRIPPER

FOLLOW UPS show that the best treatment to date for varicose veins after ligation of their source of filling (commonly the sapheno-femoral and sapheno-popliteal junction) is stripping out the defective saphenous trunk. The remedy of stripping introduced by Mayo in 1906 and Babcock in 1907, has been resuscitated Myer's stripper is excellent and a modification of it has been used with satisfaction for over a year It has a larger stripping end with a cupped face and key end behind it while its tip is available in several sizes



Modified stripper

The cupped face prevents the stripper from being pulled entirely through a large vein without stripping it or perhaps turning it inside out both of which occur with the Myer stripper The key on the end is to rotate the stripper to and fro, to facilitate its passage along an enlarged vein with pouched varices

I am indebted to Mr Millard for his skill in effecting the alterations

London W 1 HAROLD DODD

Reviews of Books

Gynæcology

5th ed Douglas H MacLeod, M S, F R C P, F.R C S, F.R C O G, gynæcological surgeon, St Mary's Hospital, London, Charles D Read, M B, F.R C S, F.R C S E, F.R.A C S, director, Institute of Obstetrics and Gynæcology, British Postgraduate Medical Federation, University of London. London J & A Churchill 1955 Pp 864 80*s*

The fifth edition of Eden and Lockyer's *Gynæcology*—the first for twenty years—has new authors but in general retains the form of previous editions Though the style of the text is unlikely to sustain the interest of the more casual reader, the graduate making a special study of gynæcology will find a comprehensive account of the subject in nearly all its aspects, with clear illustrations many of which are new The best sections are those on the more important conditions with which the gynæcological surgeon has to deal—e g, ectopic pregnancy, carcinoma of the uterus, ovarian cysts, and prolapse—and the short operative section is excellent Some topics, however, are covered at perhaps unnecessary length while others get almost cursory treatment Three pages are given to hydatid disease, and two to actinomycosis of the pelvic organs—conditions seldom encountered in this country—whilst only three short paragraphs are given to the common monilial infection of the vagina Further, the accounts of the ætiology, pathology, and elementary bacteriology of various gynæcological lesions are in general extended and elaborated at the expense of clinical features and treatment Thus in a section very properly devoted to appendicitis, there is much on the elementary anatomy and structure of the appendix but only a few sentences on the symptoms, which are described as " those of an acute abdomen, which do not call for detailed description " Sometimes, indeed, treatment is dealt with in summary fashion, and only one opinion is given For example, no more is said about the treatment of carcinoma of the vulva than that " radical vulvectomy with radical excision of the inguinal, femoral, iliac and obturator lymph nodes offers the only prospect of cure The tumours are peculiarly resistant to radiation " While this is a good working rule, the postgraduate might welcome more

The treatment of paralytic ileus is described as consisting in " measures to restore the muscular contractions of the intestine Purgatives, colon irrigation by high enemata, and the use of certain drugs such as acetylcholine and prostigmine, which act powerfully upon intestinal peristalsis, are the methods of choice " Apart from the substitution of acetylcholine for ' Pituitrin,' this statement is what appeared in the 1920 edition of the book, and it is not in accordance with current surgical thought

The detail given on most gynæcological subjects will be useful to anyone who wishes to go beyond the more elementary textbooks, and besides what he is offered here the reader will find helpful suggestions for additional reading

The Visual Fields

A Study of the Applications of Quantitative Perimetry to the Anatomy and Pathology of the Visual Pathways Brodie Hughes, M B Lond, CH M Birm, F R C.S, professor of neurosurgery, University of Birmingham Oxford Blackwell Scientific Publications 1954 Pp 174 35*s*

A comparison with the late H M Traquair's famous monograph is inevitable, and Professor Hughes pays a warm tribute to the inspiration and guidance he has received from it His own book, however, does not attempt to be an exhaustive review of the literature on the visual fields (indeed his references are sometimes less than adequate), and his emphasis, unlike Traquair's, is not on the ophthalmic aspect He deals instead with his own experience as a neurosurgeon, and his clinical observations have clearly been of unusual consistency and accuracy

His book is well arranged written in well-turned English and pleasant and easy to read, yet is crammed with [illegible]trated information The illustrations are clear, the paper good, and the print adequate even for a presbyope It can be strongly recommended, particularly to postgraduates studying for the higher diplomas

The Cerebrospinal Fluid

S Lups, M.D, medical director, Municipal Hospital, Rotterdam, A M F H. Haan, M D, head of the biochemical, cytological and bacteriological laboratory, Sanatorium Orange Nassau's Oord, Renkum Amsterdam Elsevier Publishing Company London Cleaver Hume Press 1954 Pp 350 52*s* 6*d*

This book gains importance because no monograph in English on the cerebrospinal fluid has appeared for some fifteen years In an informative introduction, Dr Pearce Bailey, Bethesda, U S A, gives a historical review, and describes the contributions of the Dutch school, especially of the University of Utrecht, to neurological art and science

The new material—much of it not yet confirmed by other workers—on the anatomy of the meninges and the biochemistry of the cerebrospinal fluid perhaps concerns the neurosurgeon rather than the clinical neurologist The colloidal reactions, which have so far received scant attention in this country, are discussed The potential risks incidental to every arachnoid puncture are underlined, and detailed instructions in technique are given in adults the authors recommend the third, instead of the more usual fourth, lumbar interspace, but point out that in infants and young children puncture should be higher, in the first or second interspace, since the thecal pocket does not descend as low as it does in adults On the other hand, there are some broad unhelpful generalisations.

Thus the section on poliomyelitis states that this disease " can be recognised early from the fluid picture when it *appears that there are fluid deviations,* e g, *pleocytosis,* the administration of convalescent serum is indicated " In point of fact, the diagnosis of non paralytic poliomyelitis, whatever the fluid findings, is merely presumptive until it has been *confirmed by the complement-fixation or kindred* test on paired sera Administration of convalescent serum in this context seems to imply use of the thecal route, though the intravenous route was probably intended (there being serious *objections to intramuscular inoculations* at this stage of the disease) Gamma globulin is now acknowledged to be safer and more potent than convalescent serum but is not without risk if given intravenously, unless well diluted

The translation has perhaps been too literal, and some clumsy constructions have resulted, but the meaning is generally plain The drawings (some in colour and many derived from previous works) are well executed and the numerous graphs clear and simple

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Genetica Medica (Rome Istituto Gregorio Mendel 1954 Pp 467 L 5000)—This book contains the papers given at the First International Symposium of Medical Genetics held in Rome in September, 1953 The occasion was the official opening of the Gregor Mendel Institute in Rome for the study of medical genetics and of twins. Contributors include Italians, French, Germans, and English, each writing in their own language, and the book provides a useful indication of the centres of activity of medical genetics in Europe In addition, the full text and translations are given of an address by Pope Pius XII, setting out the views of the Roman Catholic Church on the ethical problems involved in advising engaged and married couples who run a risk of having children with a *genotically* determined abnormality

Cardiac Symptoms in the Neuroses (2nd ed London H K Lewis 1955 Pp 50 6*s* 6*d*)—Dr *Doris Baker's* 50 pages of information about the functional cardiac symptoms of left infra mammary pain, palpitation, and sighing respiration are easy to read, and pack in the facts as they are seen and analysed in a cardiac clinic New theories and findings about the mechanisms producing these symptoms are discussed briefly, and there are interesting case histories The little section on management is not encouraging physical reablement and drugs have not proved helpful, and though Dr Baker mentions psychiatry it is without much confidence The best hope lies, she thinks, in getting the patient as fit as possible and helping him to adjust himself to his lot

THE LANCET

LONDON SATURDAY, JUNE 11, 1955

The Outlook for Poliomyelitis Vaccination

Few can have foreseen the consequences of the encouraging report two months ago on last year's trial of poliomyelitis vaccine in the United States. The vaccine was hailed by newspapers as one of the greatest medical discoveries of the century, and the conquest of paralytic poliomyelitis was celebrated. The U.S. Public Health Service authorised the production of vaccine by six commercial firms and relaxed its standards of safety testing. In an incredibly short time an ambitious programme to vaccinate millions of school children this year was well under way. But within a few days there was bad news. A number of children who had received vaccine prepared by the Cutter Laboratories fell ill with paralytic poliomyelitis and the U.S. Public Health Service immediately banned further use of vaccine from these laboratories pending investigations. Figures recently published[1] say that there were 59 cases of paralytic disease and 10 of non-paralytic disease among 400 000 children given Cutter vaccine, and the attack-rate among these children was significantly greater than would have been expected judging from the rates in previous years. In 80% of the paralytic Cutter cases paralysis first appeared in the limb in which the injection was given, and type 1 virus has been isolated from 15 persons who had *poliomyelitis after having Cutter* vaccine. After the early post-vaccination cases there came a sequence of stops and starts in the vaccination programme, coupled with unconvincing assurances that the vaccine was safe and effective and suggestions that some short-circuiting of important controls had taken place. Up to the end of last week a total of 114 cases of poliomyelitis had been reported among vaccinated people, and there had been 60 cases of poliomyelitis, including *42 of paralytic disease, in family* and other close contacts of those who had the vaccine.[2] Of these contact cases 35 (mostly paralytic) were connected with Cutter vaccine. A common sequence of events was a feverish illness or sore throat in the vaccinated child six to fourteen days after vaccination, followed after a similar interval by paralytic or bulbar poliomyelitis in a contact.

That so high a proportion of the post-vaccination cases involved children who had had *one of two* suspect batches means (when considered with the other evidence) that the most likely explanation is that some of this vaccine contained live poliomyelitis virus which had not been completely inactivated by the formaldehyde treatment.[3] But there are conflicting reports of the results of laboratory tests of the Cutter vaccine itself. One report speaks of failure to isolate live virus from the Cutter vaccine,[1] while a second[1] mentions that in one laboratory paralytic poliomyelitis had developed in one of the inoculated monkeys. Most reports state that there is no obvious way in which the preparation and testing of the two suspect batches of vaccine differed from that of other batches from the same or other firms. Faced with this difficult situation the U.S. Public Health Service has made thorough investigations of the methods of preparing vaccine in all six laboratories and after lengthy consultations it has decided to impose stricter safety standards for the manufacture and testing of vaccine. The new standards require, among other things, the presence of a United States public-health inspector in the plant of each manufacturer.[5] The firms concerned, after protesting that the new tests would be too elaborate and costly,[4] have now agreed to the measures recommended, and the interrupted vaccination programme will probably be resumed soon. It is reported that about 70% of the children whose parents had earlier agreed *to vaccination are still* ready to be vaccinated,[4] but the original programme must now be curtailed because sufficient vaccine will not be ready in time.

Assuming vaccine were freely available in this country, what should a doctor say to an anxious parent who asks whether he can recommend this vaccine for his child? Is it safe and will it protect against paralytic poliomyelitis? In the present state of uncertainty he would be forced to reply that there is unfortunately a very small but definite risk that the vaccine may produce paralytic poliomyelitis. This risk may be reduced to something extremely small by the improved tests of the vaccine in tissue-cultures and in monkeys, but there will still be the fear that the tests may not reveal the presence of every live virus particle and that the occasional highly susceptible child may be given the disease by a vaccine which has passed the most rigorous testing. This risk must be weighed against the benefits, which at the moment seem to be a three- or four-fold reduction in the chance of getting paralytic poliomyelitis in the year following vaccination—with presumably some protection for a much longer period, although the extent and duration of this are not yet known. In addition (as we have previously pointed out[6] [7]) there is a risk, of unknown dimensions, that repeated injection of a vaccine prepared from monkey kidney may eventually sensitise the child in some harmful way. This could conceivably have more serious consequences than the accidental infections on which attention has naturally been fixed so far.

What lessons can be learnt from this experience? At least we can now see the danger that lies in publicity, on the modern scale, for a method of prevention or treatment which should still be on probation. We can see that such publicity may force all concerned to apply the method immediately and widely and may leave doctors little opportunity to make up their minds on how to advise their patients. That we in this country were not constrained into premature action was partly perhaps for lack of opportunity and partly because the word poliomyelitis has not yet so menacing a sound here as it has in the United States. In every country—our own included—people are looking to vaccination as the answer to poliomyelitis and all will join in the hope that the present setback may be no more than temporary Something may be gained perhaps from the need to think again. There is as yet no reason to believe that the present vaccine is the most effective which can be produced, and it is possible that, in the end, attenuated virus may prove more satisfactory When the time comes to test this possibility, the happenings of recent weeks should ensure that enthusiasm does not carry us too far before we are ready

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[1] New York Times May 20 1955
[2] Manchester Guardian June 3 1955
[3] Lancet May 7 1955 p 936
[4] New York Times May 28 1955
[5] Ibid May 30 1955
[6] Lancet 1954 ii 851
[7] Ibid April 23 1955 p 851

Antacids for Peptic Ulcer

IN the absence of firm knowledge about the causes of gastric and duodenal ulcers the medical treatment of patients with these conditions is largely symptomatic The main symptom—pain—is usually at once relieved by reducing the acidity of the gastric contents, and much thought has been given to developing means to this end

Attempts to reduce the concentration of acid secreted have met with indifferent success Drugs given for this purpose have included atropine, methantheliniuim, and propantheline, but their efficacy is questionable An indirect approach, consisting in administration of antacids, is more reliable Patients with duodenal ulcer usually have high gastric acidity, and commonly pain is felt when the stomach is nearly empty In patients with gastric ulcer, on the other hand, the pain is usually felt when the volume of the gastric contents is greater, but the acidity of the contents is likely to be low[1 2] Thus, whether the gastric contents are highly acid or not, the amount of acid to be neutralised at any one moment is likely to be small The patient is usually satisfied to take antacid intermittently, to prevent or control pain, whereas his doctor may wish him to take it continuously, to keep gastric acidity constantly in check Usually the stomach secretes acid continuously throughout the day, and so a single dose of antacid has only a transient action[3] HUNT and MACDONALD[4] found that when the volume of the gastric contents becomes small, emptying is quick, and at the end of an hour only a small proportion of a dose of antacid will still remain in the stomach More continuous action may be secured by an intragastric drip of antacid, but sucking antacid tablets is no less effective, and during sleep the action of a single large dose of antacid may be prolonged by administering a drug, such as tricyclamol, which delays passage of the antacid through the stomach[5]

The ideal antacid should take up acid in the stomach, give it up in the intestine, and remain very insoluble during its passage through the alimentary canal Polyaminostyrene, which is a long chain aromatic base, is one substance that seems to satisfy these requirements but its capacity to absorb HCl is greatest below pH 2 5 and is very small at pH 3 For this reason it does not seem to be highly suitable for use as an antacid, but in Norway some clinicians[6 7] are convinced of its value, and its advantages should certainly be further tested The more usual antacids may be divided into two main classes First there are those—for example, sodium bicarbonate or magnesium oxide—which neutralise part of the acid secreted by the stomach by virtue of their content of potential OH^- ions and thus deprive the body of acid If the amount of acid neutralised exceeds the daily production of metabolic acid the urine will become alkaline, or if the kidneys should fail to compensate completely for the intake of OH^- ions the alkali reserve may begin to rise The seriousness of such alkalosis may have been exaggerated,[8] but there seems to be no reason for using drugs which are potentially dangerous if others equally effective are available Antacids in the second class, such as aluminium hydroxide, do not neutralise the H^+ ions of the gastric secretion, but merely adsorb or buffer them in the stomach and release them in the intestine, where the pH of the contents rises Thus with these there is no possibility of disturbing the *milieu interne* by the addition of OH^- ions Aluminium hydroxide has the additional merit that even in large quantities it will not make the gastric contents more alkaline than pH 7 The optimum acidity for the healing of gastric and duodenal ulcers is not known, but it would seem reasonable to aim for acidities between pH 3 and pH 7, corresponding to less than 1 m.eq of free acid per litre At such acidities the activity of the pepsin in the gastric contents is considerably reduced or is abolished DOUTHWAITE and THORNE[9] found that after ordinary food between 9 and 36 m eq of alkali per hour reduced the acidity of the gastric contents to pH 3 or less, without making the contents alkaline

Buffers, such as aluminium hydroxide, probably have advantages over alkalis, such as magnesium oxide, but the most important practical point is the method of administration Sucking antacid tablets because it continuously controls gastric acidity, greatly preferable to intermittent doses of antacid

Thought for the Patient

THE surgeon who is not concerned with his patients' comfort would be hard to find, it is neverthele profitable to take stock in this matter To ask our selves whether the patient is comfortable is to approach the issue wrongly We pass the bed of a patient who has had an abdominoperineal excision Is he comfortable ? Well, no he has had a big dissection in the pelvis and no better can be expected, besides morphine is giving him relief So run our thoughts as we move to the next bed If instead we ask, "In what way have I caused this patient unnecessary discomfort ?" then the train of thought covers his whole stay in hospital Before operation it was reasonable to submit him to a prick in the finger to make sure he was not anæmic But what of the venesection to discover the state of his electrolytes ? Since he had had no diarrhœa, had not vomited, was taking his food, and was passing urine satisfactorily, may not fashion have dictated this ? True, it only involved the insertion of a needle, but this can cause alarm to some, while others (including some surgeons) prefer pain to the peculiar sensation caused by a needle Investigations exhaust a patient, so the fewer the better, a trip to the X-ray department

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[1] James A H, Pickering G W Clin Sci 1949, 8, 181
[2] Atkinson M, Henley, K S *Ibid*, 1955, 14 1
[3] Douthwaite A H *Practitioner*, 1954, 173 46
[4] Hunt J N, Macdonald I *J Physiol* 1954, 126 459
[5] Aylett P Douthwaite A H *Brit med J* March 19, 1955 p 691
[6] J *Tidsskr norske Lægeforen* 1952 72, 120
[7] J *Svensk a Läkartidn* 1955, 52, 263
[8] van Guldsenhoven G M T Gray, O V, Price, A V, Sande P H *Clin Sci* 1954 13 383
[9] Douthwaite, A H, Thorne M. G *Brit med J* 1934 1 1

is easily arranged but a moment's thought may reveal that the investigation sought will shed little light on the diagnosis or the patient's ability to withstand operation.

Often convention robs us of insight so that we fail to question the value of what we are doing Time was when the bowels were purged as a routine before every operation, fortunately this practice has now virtually ceased But what of pubic shaving ? None will question the need for it before any operation on the anterior abdominal wall, but the pubic hairs are unlikely to contaminate wounds in the perineum, and yet for the patient with piles to be ated or a fissure to be excised they are usually removed together with those at the anal verge ubic shaving is not only acutely embarrassing for any, but a source of discomfort as the hairs grow un. Postoperative pain is directly related to the gree of trauma at operation heavy retraction, nt instead of sharp dissection, suturing under nsion—all these enhance discomfort How often we do all we can to avoid them ? Because time often against surgeons pushed by long lists and gthy operations small insults to human tissue y pass unheeded WILLIAMSON,[1] when removing eptic appendix, tried the exasperating experiment avoiding unnecessary trauma the operation took hour and twenty minutes, but the patient had so le discomfort that she insisted on returning to rk on the fourth day Anæsthesia is doubtless ier to control through an endotracheal tube, ich may therefore be used more often than is ictly necessary even though it leads commonly soreness of throat and sometimes to hoarseness voice Then again, the clips which fasten towels skin on occasion cause more discomfort than the ound itself To the surgeon the position of the tient on the table is of paramount importance, t the position for the best access and exposure y not be best for the patient The gall bladder n be removed from the deepest abdomen without orting to the bridge which hyperextends the ne and causes considerable backache later, and e deep Trendelenburg position, beloved of pros ectomists and gynæcologists is a positive danger arteriosclerotic patients

Why do we allow tradition still to dictate to us a tourniquet shall be placed at the end of the d of a patient whose leg has been amputated ? ondary hæmorrhage after this operation is now eard of and displaying the instrument can only e disturbing thoughts in the patient's mind t perhaps we err most when we have recourse parenteral fluids Gastrectomy completed without ident and with reasonable expedition leaves the tient so little disturbed as to need no intravenous boost' and fluids may be given by mouth within lve to twenty four hours but all too often an travenous infusion is started for the surgeon's the anæsthetist's comfort of mind How often, o, does the house surgeon cut down on the saphenous in regardless of the disability which sometimes ues, because it is easy to find or deprive the tient of the use of his right arm, simply because t has not had the foresight to choose the left for needle or cannula—and then place the whole arm in a splint, with the elbow in extension, l not arranged the apparatus so that the be inadvertently displaced ? The heinous offence using a vein in the cubital fossa is still committed (for this one senior physician used to fine his house-physicians ten shillings) When using blood our responsibility is not only to the patient, the donor should also be borne in mind Before central blood banks were started extravagant use of blood was less likely because donors had to be bled at hospital they came to our aid and were under our care Now no-one at the hospital meets the donors or has to bleed them Suppose that before a major operation three pints are ordered, just to be on the safe side It turns out that only one is needed, and two remain in the refrigerator It may be possible to use these another day—or it may not Yet to give this blood two volunteers have suffered personal inconvenience and even discomfort Letters posted in London during the month of May bore the cancellation mark Blood Donors are Still Urgently Needed

Annotations

THE STORY OF THE R S.M

IN a broadcast on May 29 Mr Donald Boyd[1] said that we English are never so English as when we are pursuing a poetic idea and added that in his opinion we are, in this day and age doing exactly that Dr Maurice Davidson, author of the official history of the Royal Society of Medicine[2] writes on the other hand, of the hard material world of today, when so much that is worth preserving is being jettisoned in the name of progress' He then settles down to describe with much spirit the pursuit of another poetic idea—that of founding a society which should embrace all the specialist societies of medicine It is a story which he notes "abounds with examples of the frustration of useful and necessary reforms by an apotheosis of outworn traditions' but he leaves his readers in no doubt that the outcome was favourable the right traditions jettisoned and the necessary reforms achieved

He takes us back to the time when Dr James Sims sat in the presidential chair of the Medical Society of London for twenty two years so much to the annoyance of more liberal minded members that twenty-six of them resigned in a body and formed, in 1805 at the Freemasons Tavern the Medical and Chirurgical Society of London These founders of the parent body from which the Royal Society of Medicine springs were a distinguished company among them being Abernethy, Baillie Cooper Marcet Saunders, and Yelloly—the last three of whom were the moving spirits in the new venture They used to meet at the Crown and Anchor until they were able to rent no 2, Verulam Buildings, which housed them for four years. After that they had various addresses in Lincoln s Inn Fields ; but in 1834 just as they received their Royal Charter from William IV their pilgrimage towards Wimpole Street brought them to 53 Berners Street and there they settled down for over half a century The Pathological Obstetrical and Epidemiological Societies met in the same street and in 1860 the Royal Medical and Chirurgical Society suggested they should all join together as one society with various sections Nothing came of this ; but in the years which followed the various societies including the Medical Society of London performed a kind of lobster quadrille some advancing, some retreating, to the tune of "Will you, won't you?"

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[1] Williamson, P Canad med Ass J 1955 72 602.

[1] *The Listener* June 2 p 975

[2] The Royal Society of Medicine The Realisation of an Ideal 1805–1955 Published by the Society at 1 Wimpole Street London, W 1 1955 Pp 201 £1 1s

In 1899 the Royal Medical and Chirurgical Society removed itself to a new house in Hanover Square, and perhaps this change, coupled with the stimulus of a fresh century, encouraged all the societies, at a conference held in 1904 at the Royal College of Physicians, to pass a resolution declaring that an effort to unite them was "highly desirable" In 1905 the long courtship was honourably concluded, the deed was done, and the various societies were united as the Royal Society of Medicine—all save one The Medical Society of London, despite its protestations of approval, in the event preferred single blessedness As Dr Davidson puts it, thus, "the oldest of the London associations of this character remains today an honoured but an independent body" Perhaps (though he does not say so) the outspoken decision of the newest society to admit women as well as men was too much for so determinedly womanless a body as the oldest

The fifty years which have passed since then have seen the steady growth, in prestige no less than size, of the Royal Society of Medicine The building at 1, Wimpole Street, opened in 1912, was enlarged in 1953 by the addition of the present fourth floor Dr Davidson tells of the founding and expansion of the famous library, the gift of the Wellcome Research Library, and the development of the photographic department which now produces microfilms, photocopies, lantern slides, X-ray reductions, prints, photographs of patients, and photomicrographs for doctors in all parts of the world He has much to say of the men who helped to establish the library, especially Sir John MacAlister "whose name and achievements seem to have run throughout the story, like a *leitmotif*" MacAlister's portrait, reproduced in the book with that of many others of the society's worthies, may not be familiar to some fellows, being hung remotely on the third floor MacAlister (a brother of Sir Donald of the General Medical Council) had been obliged by ill health to give up his medical training, and instead trained as a librarian He became the principal resident officer of the Medical and Chirurgical Society, and played a great part in bringing about the union of the societies He started the library, edited the *Proceedings*, and promoted the Fellowship of Medicine, and Dr Davidson believes that the society probably owes more to him than to any other who has worked for it Nevertheless he gives due honour to the other great names, and includes a short account of every president In one particular, however, he disappoints the reader he does not disclose the identity of the "Robert Barnes" who gave his name to the society's principal hall—a puzzle which has teased many a member

In commemoration of its 150 years' of life, first as the Royal Medical and Chirurgical Society, and since as the Royal Society of Medicine, the society held an anniversary dinner on June 7, at which the Duke of Edinburgh received the honorary fellowship and was presented with a specially bound copy of Dr Davidson's book

ORBITAL RADIOGRAPHY

ORBITAL tumours are an important diagnostic problem, for if untreated they inevitably damage the optic nerve and eventually disorganise the contents of the orbit Because of their varied origin—from within the orbit itself, from the paranasal air sinuses, or from the intracranial cavity—the clinical manifestations differ widely in the early stages when a timely operation may preserve vision At this time the tumour often presents an inconclusive picture to the rhinologist, the ophthalmologist, or the neurosurgeon, and the need for some reliable method of localisation is clear Simple radiography of [illegible] it is seldom informative, and from time to time [illegible] unig and Herrenschwand in 1927 first described the technique of injecting air into the episcleral space, efforts have been made to delineate space occupying lesions in the orbit radiographically by injecting contrast media

Cowie and Groves [1] have now found that the best contrast medium is diodone, which is readily soluble, permeates the orbital tissues, provides good contrast, and is not highly irritant Experiments on the cadaver showed that the fluid could be injected so as to fill the episcleral space, the muscle cone, and each of the four quadrants comprising the peripheral surgical space which surrounds the muscle cone, and repeated trials led to recognition of a typical normal appearance when this space is displayed radiographically In further experiments with a preplaced "tumour" of injected cocoa butter a filling defect appeared

17% proved the lowest concentration of diodone that produced reliable radiographs, and this strength (with 4% novocaine as diluent) has been used in 4 cases of orbital tumour In each a filling defect was demonstrated The reliability of this finding has been verified surgically in 1 of the cases, in 2 others the radiographic finding supports the clinical diagnosis, and in the 4th the tumour outlined in the radiographs is to be treated surgically

Experience with this method is still slight, but it may prove valuable for localising not only orbital tumours but also (judging by the experience of Cowie and Groves) certain types of intra ocular foreign body

UTERINE ACTIVITY AND ELECTRICAL RESPONSE

IN the ten years since Dill and Maiden [2] reported their observations, interest has grown in the possible clinical value of records of the electrical activity on the abdominal surface immediately over the uterus during parturition This activity consists in a fluctuating potential with mixed rhythms of shorter duration than that of the uterine contractions Potential differences of 3–10 millivolts are present, and in general the amplitudes are greater during contractions Halliday and Heyns [3] have studied these electrical changes in over 500 patients and have reached some quite unexpected conclusions The conclusions are based on statistical averages, but significant χ^2 factors indicate that the recordings could be used with 95% certainty in the diagnosis of certain conditions

Their findings, they say, provide "some support to the theory that the potentials being observed are an indication (even if indirect) of the expenditure of physiological energy in the process of labour Therefore, it is possible to suggest that when no potentials are observed the patient is not in true labour, and that the contractions will not produce dilatation of the cervix, even though the abdomen is hardening rhythmically" They find no relationship between electrical intensity and length of labour, but they do find a significant connection between such intensity and the rate at which a patient becomes exhausted

That electrical activity should be proportional to progress in labour and not to the rise and fall in uterine tension is surprising, but Steer in the U S A came to much the same conclusion It is known that a single smooth-muscle cell exhibits a change in polarisation concurrent with isometric or with isotonic contraction Moreover, large electrodes placed on the exposed uterus or on isolated strips of uterine muscle collect potential charges concurrently with general or local contraction In such cases anoxia or oxytocic drugs increase the electrical activity The electrical rhythms are rapid and resemble those found on the abdominal surface by the electrohysterograph

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1 Cowie J W Groves J S *Brit J Ophthal* 195[illegible] 39

2 Dill L V Maiden R M *Amer J Obstet Gynec* 1946 [illegible] *Ibid* 1948 56, 213

3 Halliday E C, Heyns, O S *J Obstet Gynaec, Brit Emp* [illegible] 62 165

If the changes recorded by the electrohysterograph are not due to uterine contractions per se to what do they owe their origin? Halliday and Heyns suggest that they may be related to the chemical changes associated with anoxia but anoxia is often present when there is no progressive labour Alternative explanations are (a) that they are due to a pain reflex (conscious or unconscious) with vasomotor changes in the skin (b) that they are of uterine origin and are present in the skin in sufficient intensity for measurement only with very strong contractions (c) that they reflect uterine retraction, about which little is known When more has been learnt about the cause of these changes the electrohysterograph may win a place in the diagnostic routine of the labour ward.

THE INFANT'S PHYSICAL ENVIRONMENT

THERE is still much uncertainty about the optimum environment for the young infant and his response to either hypothermia[1] or over heating This uncertainty is particularly great in the case of prematurity Here animal research is of limited value since immature animals almost invariably succumb But in their brilliant work on retrolental fibroplasia Ashton and his colleagues[2] made use of the relative immaturity of the newborn kitten's eye to demonstrate the effects of exposure to high oxygen concentration In studying the very young the veterinary surgeon with larger litters and quick turnover has many advantages over his pædiatric colleague and his observations often have a bearing on problems of *infant management*

The neonate can undoubtedly withstand a degree of anoxia that would be lethal to an older child and this, together with his surprising resilience after surgical operation has led to a change in outlook Whereas our predecessors literally wrapped him in cotton wool the new generation tends to believe that he can stand almost anything. But his survival does not necessarily mean that he has passed through an experience unscathed

Kahn and Walker[3] studying African infants, showed that sweat secretion was impaired in those with malnutrition, and that in hot weather this impairment might be associated with fever They exposed infants with kwashiorkor and healthy controls to conditions of heat and humidity such as are found in the poorer African dwellings in hot weather, and determined the response of the sweat glands quantitatively In the malnourished babies the degree of œdema was not strictly related to diminution of sweating but their ability to secrete sweat returned with improved nutrition The findings of Kahn and Walker are supported by the veterinary experiments of Clark and Quin[4] who studied the heat regulating mechanism in merino sheep They found that food intake had a direct effect on the sheep's ability to maintain body temperature during exposure to cold response to hot environment also depended largely on general body condition thin sheep on a poor diet showed suppressed panting reflex and excessive rise in temperature Bower[5] studying the peripheral vasomotor control in healthy children showed that even in normal full term neonates the rise in skin temperature in the other limbs on immersion of one limb in hot water followed a curve different from that obtained with normal infants over three months of age In the very young baby the response was much more sluggish and in almost every case the maximum skin temperature was lower

These reports teach a useful lesson—namely that the neonate is delivered to us at body temperature but is handicapped by poor vasomotor response and a relatively large surface area If he is premature these handicaps are exaggerated With satisfactory feeding each day that passes sees further adjustment to the new environment but even in later infancy the relative instability of the young child may be made evident again by illness infection or malnutrition

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[1] Mann T P *Lancet* March 19 1955 p 613.

[2] Ashton N, Ward B, Serpell G *Brit J Ophthal* 1953 37 513 see *Lancet* 1954 i 80 *Ibid*, 1954 ii 275

[3] Kahn, E Walker A R P *Pediatrics* 1954 14 650

[4] Clark R Quin J I *Onderstepoort J vet Sci* 1947 21 31

[5] Bower B D *Quart J Med* 1954 23 215

THE SOLITARY PULMONARY NODULE

THE widespread use of chest radiography has led to increased interest in the isolated pulmonary nodule unassociated with symptoms[1–10] and Wilkins[11] has now analysed a series of 77 such cases 27 proved to be primary pulmonary carcinomas 6 metastatic carcinomas 18 tuberculous lesions, 21 benign tumours or cysts, and 5 inflammatory processes of various kinds

When an isolated nodule is found the pressing question is whether it is a primary pulmonary carcinoma, because if it is, delay in diagnosis may cast away the possible chance of survival offered by resection In patients below the age of 30 carcinoma is unlikely the chances increase with advancing years, and in Wilkins's series 50% of the lesions in patients over 50 years were proved to be malignant Tuberculosis is commoner in younger patients, but is by no means rare even in the aged Simple cysts and tumours may also be discovered at any age and although some of them have favourite locations in the lung fields this is an uncertain guide because carcinoma may originate in any site Areas of calcification in the lesion (sometimes demonstrable only by tomography) suggest a tuberculoma or hamartoma, but a carcinoma may arise in or near a calcified scar Such generalisations are therefore of limited diagnostic value and a more direct approach is often equally unrewarding The lesion is usually beyond bronchoscopic vision and the finding of no tubercle bacilli or cancer cells in the sputum and bronchial secretions does not help in diagnosis. If the lesion is near the pleura aspiration biopsy may seem the easiest way of resolving doubt but this investigation is best avoided because of the danger of implanting malignant cells in the needle track Inquiry regarding previous radiographic examination of the chest may be more rewarding than elaborate investigations for the recent appearance of a lesion—particularly in an elderly man—has a sinister significance In the majority of cases exploratory thoracotomy is necessary for exact diagnosis and since the risk is trifling compared with the danger of temporising with a possible bronchial carcinoma Wilkins and all others with experience in the subject urge that this operation should be done without delay Naked-eye inspection of the nodule or examination of frozen sections will determine its nature, and thus the extent of operation Even if the lesion turns out to be non malignant most would agree that it will have been 'nane the waur o' a hangin' although many would nowadays be satisfied with probation for a tuberculoma in a young patient

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Mr GEOFFREY KEYNES and Sir LIONEL WHITBY have been appointed Sims Commonwealth travelling professors for 1956 Mr Keynes will visit Canada and parts of Africa and Sir Lionel Whitby Australia and New Zealand

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[1] Effler D B Blades B Marks E *Surgery* 1948 24 917

[2] O'Brien F J Tuttle W M Ferkaney J E *Surg Clin N Amer* 1948 28 1313

[3] Burden, W F *Amer Rev Tuberc* 1950 62 512.

[4] Davis, E W, Klepser R G *Surg Clin N Amer* 1950 30 1107

[5] Sharp D A Kinsella T J *Minnesota Med* 1950 33 886

[6] Abeles H Ehrlich D *New Engl J Med* 1951 244 85

[7] Effler D B *Amer Rev Tuberc* 1951 63 25[illegible]

[8] Harrington S W *Dis Chest* 1951 19 [illegible]

[9] Hood R T jun, Good C A, Clagett O T McDonald, J R *J Amer med Ass* 1953 152 1185

[10] Storey C F Grant R A Rothmann B F *Surg Gynec Obstet* 1953, 97 95.

[11] Wilkins E W *New Engl J Med* 1955 252 51[illegible]

Special Articles

THE HANDICAPPED ADULT IN THE COMMUNITY *

J B M Davies
M.D Lond, D P H
DEPUTY MEDICAL OFFICER OF HEALTH FOR LIVERPOOL

When the handicapped child leaves the care of the local education authority his future is considered by the employment officer, usually with sympathy but seldom in cooperation with the school medical officer Yet decisions must be made at this stage which will decide the child's whole life, and it would be logical for his teachers and the school medical officer, who have steered him through school life, and also the welfare officers who will have to help him later, to be consulted

Basically the problems of the handicapped are medical, capable of true understanding only by doctors, and this is recognised while the child is at school It is the school medical officer, and not the educationalists, who decides whether a residential or day school, a special class or home teaching, is the answer to the child's problems It is the more surprising, then, that the handicapped adolescent does not always continue to be handled by doctors His handicap is unchanged, and his problems are increased as he tries to adjust himself to his new way of life But at the time when there is greater need for medical control, that supervision is relaxed and often removed

Under most large local authorities the medical officer of health is also principal school medical officer, and this ensures that the preschool child's welfare is integrated with that of the school child It is less usual for the M O H to have charge of the welfare services, but, where he does, he and his staff can continue to supervise the handicapped child's life after he leaves school

Even where local administrative arrangements do not favour this cohesion, I believe that each handicapped child—particularly the physically handicapped and delicate children—should be individually considered at the age of 11, when he starts his secondary education, by a panel of his teachers, the school medical officer, the employment officer, and the welfare officer

The Right Job

The chances of success in a job depend on the attitude and character of the handicapped person, on the degree of handicap, and on the energy and approach of those who have to help him Often success is attained only by ingenuity and improvisation The seriously handicapped sometimes achieve great success, while others with minor handicaps fail But, irrespective of the type or degree of handicap, an individual assessment is necessary, and this can only be properly carried out by someone who visits the handicapped person at his home to see the conditions under which he must live

Who should do this assessment? Usually in the case of the blind, and the deaf and dumb, the visit is paid by someone with experience of dealing with the particular handicap With other handicaps the welfare visitor or health visitor carries out this work, often with the help of a hospital almoner, and I can see few drawbacks and many advantages in using general visitors for this purpose, at any rate in the first instance A specialised worker can be consulted later if need be By using general welfare visitors, it should be easier to ensure that the handicapped are being treated as nearly as possible as normal individuals, and more uniformity of treatme between different groups of handicapped people could maintained

Sheltered Workshops

For many of the handicapped—too many, in my vi —jobs will be found in sheltered workshops Becau costs are rising, many of these workshops are facing crisis

The main reasons for rising costs are increased wag and increased competition This latter problem is ve interesting, for it shows one of the fundamental wea nesses of the present workshop system The difficulti of the workshops of the blind are typical of many sheltere workshops today

The trades practised by the blind are traditional- basket-making, mat-making, brush-making, and machin knitting Most of them were selected at the beginnin of the century, and few have been added Yet workin conditions in open industry during this period hav changed radically For instance the cheapest brushe are now machine-made and their quality is as good a and often better than, that of hand-made brushes. It i impossible for any blind workshop to compete wit machine-made brushes, and to sell their products the may have to do so at a loss

A new entrant into a workshop is patiently taug his trade Once he is fully trained, he is accepted as worker in that trade for the rest of his working lif which may be for the next forty-five years If, durin that period, his trade becomes out of date (as has ha pened with hand brush-making) he has to continue i an out-of-date trade, or else try to learn a new one T a severely handicapped person, this may be difficul and no public body likes to put him off work just becau his trade is out of date He usually carries on his trad and through no fault of his own, continues to add to t financial burdens and difficulties of the workshop Fe would wish to disturb any blind worker who has be working satisfactorily for many years at brush mak even if this is now unprofitable; but it is wrong not face the fact that the present system is at fault A fi step should be to stop anyone else being taught t unprofitable trade, but even this has not been accep throughout the country

No one can say for certain whether or when an occup tion suitable for a handicapped person today will n become out of date Where, then, is the answer to th awkward question?

It must be recognised that any sheltered worksh however efficient, will run at an increasing loss Th being so, an even smaller proportion of the disab should be sent to them—not only because of the expe (though it is no use pretending that expense can ignored) but because they will never provide the answ to the main problems This in my view can be found o in open industry At present the handicapped entra into industry, after an initial training, has to pull weight in competition with other workers Each is plac with great patience on the part of the placement office naturally careful selection has to be ensured, and the who are successful in open industry are the happiest handicapped workers The main difficulty in industr placing of a handicapped class is not so much that suitab *occupations are not available*, as that initially th employer cannot afford to employ them The difficulty is met in sheltered workshops, and it is o by considerable augmentation that any workshop ca continue The obvious answer seems to be that augmen tation should be introduced into open industry Toda in Liverpool, for instance, each worker in one of o workshops for the blind costs over £5 a week If w could go to prospective employers in open industry, a offer to augment up to, say, £2 a week, I believe placements would be numerous enough to solve a su stantial part of the problem Of course there are di culties—the complaint of unfair competition, for example But none of these are insurmountable Only a small number of people are involved, and a few industrial firms have already shown that severely disabled persons can do efficient work

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* B[illegible]d on a paper given to the Society of Medical Officers [illegible] th on Nov 5, 1954

Even if such a suggestion were accepted, there would still be a place for sheltered workshops. But their numbers should be kept to a minimum and they should cater mainly for two groups

(1) Severely disabled whose only hope of full time employment is in sheltered workshops. This should be a small group and should not contain people unable to work full time

(2) A less severely disabled group who are training to enter industry A reasonable time-limit must be placed on their stay and they should not be allowed to drift into the first group.

Those who are in charge of sheltered workshops complain that they are unable to find suitable new skilled trades. But there is another approach to this subject which seems more promising Most of their difficulties arise from competition, which may make a trade hitherto lucrative to the handicapped no longer so attractive The only way to avoid this is for workshops not to be tied to skilled trades at all The Tuberculosis Colony at st Barrow successfully employs handicapped persons in any suitable unskilled work which is available at the time Packing components in tropical packs and dismantling out-of-date wireless equipment have provided work for many years They are prepared to do work for which there is demand at that time and by not tying themselves to any fixed trades they avoid the snags and difficulties of any occupation becoming obsolete

At first sight this may seem a retrograde step for it would deprive the handicapped of the opportunity to learn a skilled trade But this is not so With a larger and larger proportion of the handicapped finding a place in open industry all these would have a skilled trade in industry Those doing the unskilled work would be the few who are employed full time in the workshops, and the real security of these workers is the sheltered workshop itself rather than the occupation they follow

Home Workers

The schemes for home workers vary greatly but since new scales were agreed to two years ago there has been greater uniformity in the system of augmentation These schemes, which are only for full time employment at home, are the only form of sheltered employment open to handicapped people living in rural areas or within small communities where it is impossible to run a workshop

The usual way of assessing full time work in these schemes is to prescribe a minimum amount of work which must be completed by each worker to qualify for augmentation It was a real advance when this system was adopted nationally in preference to the method of fixed augmentation, paid irrespective to output Many of the home worker schemes are not anything like so costly as sheltered workshops and they are working satisfactorily in country areas

The arguments for preferring open industry wherever this is possible still apply to this group, but undoubtedly home worker schemes will always be needed. Perhaps the greatest dangers of these schemes is that augmentation may be offered to part-time workers which would upset the whole concept of augmentation By ensuring a reasonable minimum output of high quality goods this difficulty can be avoided

Occupational Therapy

Part time work comes really into the sphere of occupational therapy Some authorities have set up a domiciliary occupational therapy service The ideal system arranges for occupational therapy to be available to as large a group as possible, including chronic sick and crippled at home those rehabilitating at home after a long illness such as pulmonary tuberculosis and the aged living in their own homes or in hostels

Such a service to be successful must have a satisfactory outlet for the sale of the goods made This problem common with all home made products is best solved by using one central shop to cater for all of them

The advantages of an occupational service are great for not only does it help and encourage many who are beginning to face the problem of overcoming their disabilities but also it is a useful link with the hospitals. Too many patients receive great help from occupational therapy while they are patients, but cease to do so on discharge The domiciliary occupational service should come into action as soon as the patient leaves hospital

Welfare Services

The young crippled adult without a home and in need of care and protection is one of the most pitiful objects today There are a few outstanding voluntary homes but unless a place in one of these can be found, he must be put in part III accommodation intended for aged people

If we are to provide a real welfare service for this group we must take over where the special school leaves off The special training colleges, such as St Loyes at Exeter, should be increased, but there should be one coördinated policy for each handicapped person If possible a decision should be made early in the child s life What is really needed is the kind of supervisory control at present exercised over the handicapped child at school The larger local authorities could provide hostels run in close association with the special schools and special training colleges

However their future is settled the welfare services will continue to play a large part in the lives of most handicapped people At present these services are very unevenly distributed Thus the welfare services for the blind have dwarfed all other welfare provision for the handicapped with the possible exception in some areas of provisions for the deaf and dumb Though the need to extend our welfare services to other groups is nowadays recognised the cost of blind welfare has in fact risen since 1948 proportionately far more than the costs of any of the new welfare services for the handicapped. In Liverpool in 1949 £9397 was spent on the blind against £6419 on the deaf and dumb the physically handicapped, and the epileptic but in the year ending March 31 1955 £25 156 was spent on the blind and £14 041 on the deaf and dumb the physically handicapped, and the epileptic—an increase of 168% for the blind compared with 128% for the other groups

There is also considerable inequality in the standard of service available at different periods of the handicapped person s life For the handicapped school-child, amenities are better than they are at any later time. To lavish all the special care of a residential special school on him and then to provide next to nothing when he leaves school is surely to have failed to understand the meaning of education

What is needed is a steady coördinated policy from school life into adolescent life and on into adult life Many of the severely crippled will not succeed unless they have help at every stage and they will very seldom get it unless the same person, administratively is watching over them all the time My own belief is that until the welfare services are everywhere organised by the medical officer of health the provisions for the adult handicapped will remain as disjointed and haphazard as they are in many parts of the country today

FOOD IN MENTAL HOSPITALS

D G Harington Hawes

SECRETARY, HOSPITAL CATERING AND DIET COMMITTEE,
KING EDWARD'S HOSPITAL FUND FOR LONDON

The tradition that mental patients need only one substantial meal in the day, and that most of them are oblivious to what they eat or how their food is served, dies hard Because of this belief the kitchens of most mental hospitals were designed, equipped, and staffed to provide a simple, inexpensive, repetitive diet, planned round a two-course hot meal at midday Reliance on patients for much of the kitchen work affected not only the standard of cooking but also the type of equipment—hence the outsize boiling pans and banks of steaming-ovens that are still to be found in many a mental hospital kitchen

Today even the most progressive and diet conscious mental-hospital management committee may well be at a loss as to how to proceed Among the obstacles to good catering confronting them may be a badly designed, ill-equipped kitchen serving 2500 meals at midday , unsatisfactory means of distributing food to the wards, aggravated by long hauls out of doors to distant villas and the absence of lifts in multi-storey blocks , ward or villa kitchens that are inadequately equipped and too cramped for a proper service of meals , shortage of trained staff in the main kitchen, coupled with a decline in the proportion of patients available for work in the kitchens , and as a final straw, a chronic lack of money for the catering department

COOKING AND SERVICE

Since the majority of mental hospitals—31 out of 47 in the four Metropolitan regions—have more than 1000 beds, and since most (if not all) of them prepare the main meals for both patients and staff in a central kitchen, it follows that very often upwards of 2500 and even 3000 midday dinners have to be cooked in the same place and at the same time Now it is generally recognised that even under favourable conditions, with good equipment and competent staff, the maximum number of meals which can be cooked in a single kitchen, without deterioration in the standard of preparation, palatability, and nutritive value, is in the region of 1500 Furthermore, in a large hospital kitchen there is the added complication that the bulk of the meals must be ready for distribution simultaneously and at a fixed time This cannot be achieved unless the preparation of some of the components of the meal is started long in advance, with all the spoiling of the food that this entails

DISTRIBUTION

When the moment for distribution comes, new difficulties arise In many mental hospitals the food is loaded into metal containers, which may or may not be insulated but which certainly are not pre-heated These containers then have to be transported to the wards, which may be in blocks or in villas Some will be a long way from the kitchen, and by the time the food has reached the ward half an hour or more may have elapsed In many hospitals the conveyance of the containers to the wards is also a problem , they must either be pulled on trolleys through the hospital grounds to the villas, or man-handled up awkward stairs to upper storey wards Even where adequate electric power is available in the kitchen, the use of pre heated electric trolleys with fitted containers is not necessarily an ideal solution, if only because of the large numbers involved The standard trolley of this kind is reckoned to carry enough food for 30 persons , so a hospital with 2000 patients will need 66 trolleys The difficulty of st nd loading such a fleet of trolleys in one kitchen comment

SERVICE

When the food takes a long time to reach the ward it may have to be warmed up, and this means delay extra work, and some loss in food value In many ward patients take their meals in a dining room or day room which is usually near to the ward or part of it Th charge nurse who has to reheat the food for 40-5 patients, portion it, and serve it on plates cannot b blamed if speed is the first consideration Though many patients may be unaffected by the conditions in whic they eat, there must be many others, especially among th voluntary admissions, who are upset by austerity crocker and slapdash service

The equipment and design of many ward kitchen needs bringing up to date, particularly by the provisio of water boilers for making hot drinks, double compart ment sinks, boiling-plates and grills, and, where food kept overnight, refrigerators The size of this proble is shown by a recent estimate that it would need £20,0 to bring the 42 ward kitchens in one large mental hospit up to standard Replanning these ward kitchens h been made more difficult by the fact that no two of the have identical dimensions

THE FOOD ITSELF

And what of the meals when they are finally served patients ? Below is a menu for a week in Novemb 1954, from a mental hospital in the Metropolitan ar with more than 2000 beds The hospital was built the 20th century, and it has a well-equipped kitchen a a progressive management committee , so it is n unreasonable to assume that the menu is at least up to average Nevertheless, the breakfasts and suppers obviously light The cost per head per week of feedi patients and staff was 15s , compared with 26s for gene hospitals in the same region

In most mental hospitals supper is finished by 6 P and for many of the patients it must be a long wait

	Breakfast	*Dinner*	*Tea*	*Suppe*
Sunday	Bacon Margarine Tea	Roast beef Cabbage Potatoes Stewed prunes Custard	Fruit cake Jam Margarine Tea	Cheese Pickles Cocoa
Monday	Eggs Margarine Tea	Boiled bacon Carrots Butter beans Bread pudding White sauce	Dessert apples Syrup Margarine Tea	Scotch
Tuesday	Porridge Marmalade Margarine Tea	Meat pie Cauliflower Potatoes Stewed fruit M. Blanc mange F Ice-cream	Jam Buns Margarine Tea	Savoury Pie Cocoa
Wednesday	Bacon Margarine Tea	Braised liver Cabbage Potatoes Currant roll Custard	Cake Syrup Margarine Tea	Brawn Mashed potatoes Cocoa
Thursday	Eggs Margarine Tea	M Fried fish Chips F Steamed fish Stewed apple Custard Lemon curd	Cheese Margarine Tea	Shepherd' pie
Friday	Smoked fish Margarine Tea	Roast beef Cabbage Potatoes Rice pudding Jam	Fruit Jam Margarine Tea (villas ice-cream)	Pea soup
Saturday	Porridge Marmalade Margarine Tea	Sausages Onions Potatoes Suet pudding Treacle	Fish paste Margarine Tea	Cheese and potato Cocoa

breakfast on a bowl of Scotch broth or a plate of pea soup The fact must, however, be faced that any attempt to give a more substantial or later supper will run up against the problem of staff Most mental hospital kitchens are worked on a single shift, concentrating on the midday meal, and with a minimum number of staff preparing breakfasts and suppers. Any improvement in ither of these meals or any postponement of the supper our must mean the employment of more cooks in preparation and more labour in distribution

In the past mental hospitals have relied on patients bour for much of the work in the kitchens, but lately is source of supply has been steadily contracting inly because of the growing numbers of voluntary tients. At the same time the difficulties of recruiting ined kitchen staff are even more acute in mental than other hospitals so even if larger kitchen establish nts were sanctioned it is very doubtful whether the itional places could be filled at the present rates of y and in existing working conditions.

The difference in the amounts spent per person per week food in mental and general hospitals is shown by the owing figures for 1953–54 in two of the Metropolitan ons

	Mental (including mental-deficiency)		*General*		*Difference*	
	s	d	s	d	s	d
on A	17	7	26	9	9	2
n B	15	9	24	9	9	0

ow the 9s is saved may be seen from the following ysis, based on figures obtained in recent surveys by Hospital Catering Advisory Service of the King's nd

Item	*Average weekly expenditure per head*				*Difference*		
	General		*Mental*				
	s	d	s	d	s	d	
	5	0	2	6	2	6	9s 3d
ry	3	6	2	6	1	0	
	1	1		1	1	0	
	1	3		9		6	
and vegetables	3	9	2	6	1	3	
rs	11	0	8	0	3	0	

se figures show a remarkable difference between standard of feeding in our mental and general pitals Admittedly there is a greater proportion of y old patients in mental hospitals, whose appetites smaller than the average On the other hand most the younger patients are ambulant and many are re compared with the great majority of general pital patients who are confined to bed

re money to buy provisions is however, only half t is required. If the other handicaps to a proper ndard of catering in our mental hospitals are to be come a far reaching programme of decentralisation re-equipment combined with an expansion and ding of catering staff will have to be undertaken r a detailed survey of all the mental hospitals could how much such a programme would cost; but ly the figure would run into millions and so long as present ceiling is imposed on the National Health ce budget these millions will not be forthcoming rtheless, the need for improvement is so pressing t it must be undertaken and when the need is great gh the means can always be found

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WEST GERMAN HEALTH SERVICES

FROM A GERMAN CORRESPONDENT

A DRAFT law lately discussed by the West German lament regularises the relation of doctors to the al social insurance offices (*krankenkassen*) This law affects in the first place doctors already on the itaire offices panel—about 32 000 out of a total of st 0 000 in Western Germany Some 12 000 who not on the panel treat private patients only and since over 80% of the population are insured, the financial position of these doctors is precarious The draft law provides for an increase in the number of doctors on the insurance offices' panel from 1 in 600 to 1 in 500 patients The doctors remuneration will be based both on the amount of work they undertake and on the financial position of the insurance office in question Doctors and insurance offices are to set up arbitration committees with a jointly elected chairman, with powers to settle disputes

The draft law does not touch the problem of reform of social insurance most doctors regard such reform as necessary Nor does it promise decisive improvement in the difficult financial position of doctors already on the panel Under these circumstances opinion in the profession is divided A small minority think it best for doctors in time, to become Civil Servants The overwhelming majority wishes to preserve the profession s independence This opinion has been expressed by a group of doctors, led by Dr Schnitt of Munich who have devised a plan of social insurance reform

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CELEBRATION AT HAMMERSMITH

May 13 1935 marked the start of a brave experiment on that day King George V opened the Postgraduate Medical School at Hammersmith L C C Hospital London There were other instances of links between teaching bodies and local authority hospitals, but none so close as this and heads were shaken wisely

In the event the association proved brilliantly successful The hospital which had been opened in 1905 as a poor law infirmary and workhouse had in 1930 passed to the control of the London County Council, and its practice was already of the standard set throughout the L C C service but the standard rose as it always does when teachers and taught assemble in wards. The school attracted a most able staff and the steady flow of students to it and of notable research from it attest to its continuing vigour

This week the hospital has been celebrating its jubilee and the school its twentieth anniversary On Monday these were visited by the Queen who was received by Mr Iain Macleod the Minister of Health

The Queen first visited the office of the Postgraduate Medical School, where she saw documents relating to the opening of the school by her grandfather in 1935 She then inspected the new metabolic unit which was opened this year and is equipped for all kinds of metabolic study particularly those relating to radiation hazards. She went to the Medical Research Council s radiotherapeutic research building opened in 1953 where she inspected the linear accelerator and pressed a button which set the whole cyclotron unit in operation for the first time She visited a gynaecological ward and a male surgical ward and proceeded to an exhibition illustrating research at the school

Among many elegantly displayed demonstrations from the department of surgery she saw an artificial heart-lung machine for maintaining artificial circulation during cardiac operations and descriptions of work on blood groups in relation to cancer and on transplantation of animal kidneys. The departments of medicine and biophysics displayed a mass spectrometer which has been designed for instantaneous simultaneous analysis of respiration gases—the only instrument of its kind in the country There was also a working model of the heart and circulation constructed for studies of the effect of valve lesions on cardiac output There were demonstrations of the investigation of thyroid function by radio-iodine and diagrams concerning work done on crush injuries during air raids advances in the treatment of malignant hypertension and investigations into the treatment of chronic bronchitis The Institute of Obstetrics and Gynaecology had demonstrations on placental localisation, studies of placental blood flow resuscitation of the newborn plasma-volume determinations, and vaginal cytology There was a large number of demonstrations from the department of pathology, including apparatus for measuring the total amount of radioactivity of a subject, which can be used for many purposes, such as the determination of the body content and exchange of sodium The department of hæmatology showed studies of hereditary anæmias, and the assay of vitamin B_{12} The department of bacteriology showed recent work on antibacterial drugs, vaccines, and bacterial genetics Lastly the experimental radiopathology research unit had a demonstration of autoradiographs and chromatography

Finally the Queen visited the nurses' home, where she signed the visitors' books of the hospital and the Postgraduate Medical School.

On Tuesday the hospital and the demonstrations were shown to distinguished visitors, and Wednesday was an Open Day

The Widdicombe File

XXV THE MERRYGOWHIMBLES

DEAR BREWER,

Lord Penballock has Sonne dysentery I use the present tense with hesitation, because I saw him and his shaggy pony (the one as weary and muddy as the other) returning from hunting today As a doctor I take this to be evidence of vigorous health, but as a bacteriologist I must believe the cultures on my bench · I do not think that his headmaster will welcome him until guaranteed free from infection , and so, at the risk of seeming fussy, we had better see three negative fæcal specimens before his return to Keate's Grove I doubt if the hardy splinter will object to the strict rules of quarantine

I know something of the origin of his infection because I was waylaid by his mother Her impudent curiosity would be an asset to any epidemiologist Beyond reasonable doubt the Honourable Anna has had the same complaint but has now returned to St Ethelberta's Her ladyship went so far as to allow that she herself had had a touch of the merrygowhimbles which she attributed to a Lithuanian recipe clipped from the newspaper Old Nanny admitted nothing—but nannies never do That, as you know, is all the household except for the daily, Mrs Gush Now my agents tell me that during the past fortnight the whole village has been troubled by a varying degree of looseness of the bowels Apples, beer, and the new baker share popular blame, but the one specimen of fæces which reached the laboratory grew *Shigella sonnei* I would have liked to confirm this by other specimens but know well enough that the calls of nature must be outrageous before we Widdicombians admit our frailty

Sonne dysentery has not had the attention which it deserves Without a pennyworth of evidence I suspect that it is a newcomer The bacillary dysentery which we heard of as students was an exotic disease limited in this country to the insane and those who lived in sordid squalor This mild but very infectious diarrhœa which lays whole regiments low in an afternoon and spares neither dukes nor dustmen was not in the curriculum It seems to have crept among us between the wars The first examples were a matter for excitement and much epidemiological activity Now we are resigned to the nuisance which it causes without knowing much more than we did It waxes and wanes for no clear cause It has been popular to attribute its prevalence to an increase in communal feeding so popular that what was an intelligent guess is now accepted as proven fact I doubt if this is all the story Soldiers, sailors, schoolboys, and convicts have eaten at a common board for years , were these stricken [illegible] dysentery when the free living world escaped ? It is too late to guess whence it came It seems pretty universal today and in warmer climates cannot be distinguished (except by the bacteriologist) from milder infections caused by other dysentery bacilli Neverthele I suspect that there is some essential difference Perhap *Shig sonnei* survives our inclement climate more easily or depends less upon flies for its transport, or the infectiou dose is smaller—or something else I wonder if it is disease which has yet to establish a steady symbiosis wit the English ?

I am expecting signals of distress from Miss Buxom St Ethelberta's Since the venerable Cobbleigh burst o laughing when she proposed to close the school beca three girls had threadworms, she turns to me for t advice which she seldom takes To her, as to many her kind, *mens sana* is less than nothing compared wi *corpus sanum* If, as I expect, Anna passes on h infection, the three Rs will give way to black draugh sulphur candles, and probably lysol baths When have said my piece on Sonne dysentery she will looking for another hygienic oracle

Most of what I know of this disease I learned du the war from a battalion of our own Royal Dartm Pioneers One morning about twenty men reported s with diarrhœa As soon as the doctor left the M.I roo twice that number sneaked in to beg a dose for t same complaint When I arrived two hours la there was still a sizable queue outside the latrin Clearly the daily sick return was not much use to epidemiologist

In those days I believed beyond doubt that an o break of any intestinal infection arose from a single sou via food or drink. (These North Devon men like B are not such boobies as we think) Since dysenter primarily a human disease, this source must be unsuspected carrier Since the explosive character of outbreak indicated a common article of diet and since water was chlorinated almost to the point of emitt green fumes, the carrier must be among the cook found him without trouble—all seven of them, of wh two had exuberant diarrhœa If any one of the se was the single *fons et origo* of the trouble I did not do not know how to distinguish him from his equ infectious fellows

The Pioneers taught me two other things Every during the preceding week one or two men had repor sick with diarrhœa This was no reason for alarm no fæces were examined, but I discovered that not of these had suffered on the fatal day In the week wh followed there were but two more infections and on these in a man who had been absent on that day E in the pride of my youth I did not attribute this mi to the hints on kitchen hygiene which I gav those pestiferous cooks Since then I have see good many epidemics of Sonne dysentery in closed co munities, and experience has on the whole confir the tentative guesses which I made in the camp Ballywillwill

I believe that for every adult sick enough to medical aid there will be two more with less se diarrhœa and perhaps four who excrete *Shig so* without evidence of infection They may do this for th days or three weeks some children seem to extend t period to three months The carrier of Sonne dysente (in the sense in which the word is used of an ente carrier) may or may not exist, but how he may distinguished from one who has suffered a recent ove hidden infection I do not know Such slight evidenc I have suggests that infection is introduced most o by such a convalescent Within the community infec spreads slowly at first, but how I do not know toilet-paper is flimsy stuff and *Bacterium coli* may found on the fingers of many of us it may be that the ordinary contacts of social life are enough to diffuse the infection *Shig sonnei* has been found in the dust under a sufferer's bed and an airborne spread is not inconceivable (I once looked at hundreds of throat-swabs with this in mind but without success) On a R.A.F station I watched the infection spread in a matter of weeks from dispersed site to dispersed site without any explosive demonstration of its presence

If symptomless infections are only half as common as suspect, the infection will be widespread before it is ticed The climax is reached when one or more of ose who cook or serve the food is infected The sick room *registers a dramatic—and deceptive—bound* The vice of the hygienist is sought, and, whatever it may it is an immediate success So too, I think, is passive unity There are no more infections because there no more susceptible subjects at risk How absolute how persistent is the immunity following infection do not know After I had had the disease I tried to ect myself for several months without result: I was bably fortunate or I would have been court martialled a self inflicted injury Not long ago I saw two demics within a twelvemonth in a home for little eciles whose habits made it certain that all the ates were exposed to infection In the first all the dren had diarrhœa except one newcomer who may introduced the infection In the second symptoms infection were limited to those children who had rived since the first epidemic Perhaps this was nce perhaps not

would not have you apply these surmises to all demics of Sonne dysentery without qualification rrhœa in an infant is an inescapable fact and I believe the proportion of symptomless infections among m is smaller When the disease is epidemic among the lation at large it is not easy to trace its spread It n the whole true that each family behaves as a closed munity—i e if one member shows symptoms most he others will be found to harbour the infection On of this the pattern *of the epidemic may be altered* by munal feeding and even in this tidy island, by rted water supplies Three hundred employees ted in one canteen catch the attention better than same number in a hundred separate homes

hat shall I tell Miss Buxom ? Experience has taught that the orthodox measures which we call hygiene are and disinfectant wasted Today or tomorrow it ht be possible to detect all those so far infected and re them. Apart from a distaste for the labour and s of examining a hundred and fifty fæcal specimens ne day I have not found this plan successful I ot detect *Shig sonnei* in less than eighteen hours knows whither it may have spread in this time ? les I am the first to admit that my methods may miss r two Since I know the nature of the infection I no point in culturing any fæces at all at this stage all not advise closing the school Apart from the se parents may reasonably object to a course h spreads the infection to brothers and sisters at Prophylactic doses of sulpha drugs have not ked in my hands nor I think in anyone else s I ld not care to dispense chloramphenicol widely and dly

shall advise Miss B to watch and pray—and to see no person with frank diarrhœa cooks or serves the d. My guess is that there will be the least interference h the normal working of the school if all the suscep es catch the disease as quickly as possible If I s logical I would omit the last part of my advice I know the difference between courage and hardiness

My part will come in four weeks time Then I shall wish to examine the fæces of the whole community at leisure and to smite those Shigellæ which linger

A hundred homes, and I do not know how many other academies will have reason to thank me if I succeed The girls have to produce a certificate of health when they return to school Parents have an equal right to such a guarantee

The telephone is ringing I wish Miss Buxom did not frighten me so

Yours sincerely

HARRY HAWKE

Medicine and the Law

Supervision in Children's Ward

A GIRL of 9, who was an inpatient in a children's ward was a walking patient and had her meals with other such children in a playroom It was a rule that they should remain seated until the end of the meal On Aug 13 1952 after the female orderly had left the children with their first course and gone to fetch the pudding the girl left the playroom, ran through the ward and suffered severe injuries when she pushed her arm through the lowest glass panel of a swing door in the ward The girl said that after the orderly left the room a boy had chased her with a dead mouse, and she ran out of the playroom into the ward and pushed open the first pair of swing doors She had looked round when about to open the second swing door and pushed her hand through the glass The boy's story was quite different he said that the girl in disobedience of the orderly had run out of the play room into the ward and swinging on the doors she had tripped over the stud used to fasten the doors back and put her hand through the glass.

In an action in the Queen's Bench Division for negligence against the hospital management committee Mr Justice Streatfield giving judgment on May 20, said that he was satisfied that these swing doors were normally kept open He did not think that the little girl was an untruthful child, but children were inclined to be imaginative especially if there were a stratum of truth in the story and there had been mice in the ward He was bound to conclude that the accident had not occurred because the girl was being chased with a mouse but because she had disobeyed the rules. Considering the duty of a hospital in supervising the children in the children s ward his Lordship said that he was not prepared to measure that duty by any more severe standard than that of a schoolmaster—namely that of an ordinary prudent parent Although he did not think that this was a case where the burden of proof was on the hospital to show that they were not negligent, he would in order to give the girl the benefit of the law consider the position as if the hospital did have that burden Lord Justice Denning in the case relating to an overturned inhaler had said that with all the skill and care that could reasonably be expected accidents and misadventures did occur

Mr Justice Streatfield thought that the hospital had provided adequate supervision in having the orderly to go to and fro and it was unthinkable that anyone should have to be there watching during her absences. If contrary to his view it was necessary for the hospital to discharge the burden of proof they had given an adequate explanation on which he would have held that they had sufficiently discharged it The action was dismissed

British Medical Association

THE association held its annual representative meeting in London from June 1 to 4, under the chairmanship of Dr I D GRANT (Glasgow) The annual meeting of the B M.A is in Toronto this year, from June 20 to 24

The chairman of council, Dr E A GREGG (London), in a summary of the association's activities, announced that a number of fresh claims had been made by the staff side of the Whitley Council for new salary scales for hospital medical officers It was regrettable that the new salary claim made on behalf of senior hospital medical officers had not found immediate acceptance In the public health field the most disappointing feature of the recent award of the Industrial Court was the apparent acceptance of the contention that the remuneration of public health medical officers should be related, not to that of other branches of the medical profession, but to that of other professional officers employed by local authorities

Dr Gregg also announced that the invitation sent to Russia last August had been accepted, and the B M A hoped shortly to entertain six distinguished Soviet doctors

The early business of the meeting included the election as vice-presidents of Dr A W S SICHEL, of South Africa, and Dr P T O'FARRELL, of Eire , and Dr ALEXANDER H HALL, of Hove, was named president-elect for 1956-57 This will be the first time since 1939-40 that a general practitioner has been president of the B.M.A

GENERAL PRACTICE

The meeting quickly got down to considering conditions of service and remuneration Dr A TALBOT ROGERS (Bromley), chairman of the General Medical Services Committee, said that the findings of the Willink Committee would have considerable repercussions on the future of general practice "We have been worried for some time at the rather unplanned way medical schools have been accepting students up to their full quota," he added Dr Rogers welcomed the precedent created over the inspection of doctors' surgeries, whereby the investigation was carried out by doctors , and he was able to announce that the Government had now agreed to raise the rate of payment to principals for trainee assistants by £75 a year

A series of motions asked for higher remuneration for general practitioners in view of the rising cost of living That from North Glamorgan and Brecknock, which called for an approach to the Minister, was selected for discussion In moving it, Dr A COLEMAN declared that the betterment factor should go up as the cost of living went up , he was dissatisfied with a variable central pool Dr H H GOODMAN (Newcastle upon Tyne) said that doctors could not, as in the past, pass on their increased costs to the "consumer" The working classes were always asking for higher wages and getting them In the North it was common for the young general practitioner to be receiving less than a miner This, too, was a question also of differentials There was a danger that what was happening on the Continent would happen in this country—the abolition of the middle classes Dr A V RUSSELL (Wolverhampton), however, pleaded "Do not let us approach this from the trade union angle" while Dr S WAND (Birmingham) pointed out that it was not Government policy to attach the higher income levels to the cost of living, and he warned that the time was not appropriate for negotiations motion was lost

Southampton division was concerned about ractice, because, Dr R M WARREN explained, they felt there was a risk of the State acquiring group practice premises as a step to a full time service Encouragement of group practices might result in a rota system, with harm to the doctor patient relationship Dr TALBOT ROGERS was reassuring, and Southampton's motion was lost

DRUGS FOR PRIVATE PATIENTS

On the subject of drugs for private patients, opposing views were heard from members of the Cohen Committee Dr F P BOOTH (Mid Cheshire) felt that drugs and appliances should be supplied under the National Health Service to private patients as a right and not as a concession Dr C W WALKER (Cambridge), a member of the Cohen Committee, drew cries of protest when he declared that this system would be liable to abuse, with debasement of State practice in order to induce more to become private patients Dr ENID HUGHES (Denbigh and Flint West) said that she was an aggressive member of the minority on the Cohen Committee who protested at this "violent injustice" The assertion in the committee's report that doctors in private practice would be unwilling to accept safeguards on prescribing was vigorously challenged Dr W WOOLLEY (Bristol) said that a questionary had been sent to 253 Bristol doctors Of the 240 who replied, the only 3 who were unwilling to accept such control were doctors who favoured a whole time salaried service , all 10 doctors who were wholly engaged in private practice agreed to such a condition Dr R HALE-WHITE (Marylebone) confirmed from his own observations that doctors in London were willing to accept control

Dr TALBOT ROGERS said that it was the wish and intention of the council to follow up the question of free drugs for private patients The meeting, on the suggestion of the Guildford division, passed resolutions regretting that no minority report in favour of the supply of drugs for private patients was issued by the Cohen Committee and calling on the council to find out how many priv practitioners concerned would be prepared to acce suitable safeguards

ECONOMY IN PRESCRIBING

Another lively subject was excessive prescribing a its penalties Dr FRANK GRAY (London) asked t meeting to reject a motion by East Kent which asked th an executive council should send a circular to gener practitioners when it became aware that a new prepar tion which was being prescribed did not appear to a drug forming part of the pharmaceutical servic no practitioner to be surcharged until this notice h been circulated Dr Gray said that this was asking a l body to tell the doctor, and the motion was lost

Dr G P HENRY (Glasgow) declared that not only th doctors but a good many of the more intelligent patie were concerned about the matter of penalties for exce prescribing The doctor was not entitled to prescri what he thought his patient needed He was entitle to prescribe only subject to what some committee other thought was an excessive drain on funds Th penalty in one case was £300 Why were men who we fined such large sums not given the option of impris ment ? Dr D F HUTCHINSON (London), howeve said that it was not a fine at all A doctor was entitle to prescribe any drug, the only caveat being that if h was called to account for his prescribing he had to justi it to the local medical committee—the elected repre sentatives of the practitioner and his colleagues alternative machinery had been suggested

Dr G D THOMPSON (Lancaster), who had heard cas a member of a committee, said that some were astound One doctor admitted that if a patient came in and for anything he got it. Another was prescribing at a rate £300 a month in excess of his colleagues—£4800 a year

OBSTETRIC BEDS

The meeting agreed that every general practitioner who desired it should have access to maternity beds Dr H N **Rose** (Stratford) who moved the motion, said that contact with hospital was necessary if the standard of domiciliary midwifery was to be kept up Dr L **Crawford** (St. Helens) and Dr R M S **McConaghey** (Torquay) described examples of successful arrangements of this kind

TRAINEE ASSISTANTS

The trainee assistant scheme came under its customary annual fire Dr H F **Hiscocks** (South East Essex) pointed to advertisements in the *British Medical Journal* "Required urgently, trainee assistant' But Dr J A. **Brown** (Birmingham) though he admitted that there had been failures, declared this was no reason to condemn the scheme as a whole The meeting thought the same and rejected a motion calling for the abolition of the scheme as ' unnecessary and extravagant.

ASSISTANTS IN GENERAL PRACTICE

Considering the report of the subcommittee on sistants in general practice the meeting agreed that assistant should enter into a written legal agreement hen accepting a post, either with or without a view partnership The subcommittee also recommended hat local executive councils should in consultation with cal medical committees, periodically review all cases in hich consent had been given to the employment of an sistant. Dr A V **Russell** (Wolverhampton) thought hat a legal agreement was all that was necessary but r **Ward** pointed out that the future of the profession as in the hands of these men—' their attitude to the ational Health Service and to a State salaried service his is very important) may be coloured by their perience in their first years as assistants The commendation was carried Another proposal was at a principal implementing a view should have the ght to claim retrospective payment on the basis of tional lists for a period up to a maximum of one ar; but this was less favourably received Dr **Joan** **appell** (North Middlesex) said that partnership like rriage should be entered into on the principle of tual regard not of financial gain The meeting ferred romance and rejected the recommendation

DISCIPLINARY MACHINERY

Dr B **Hirsh** (Manchester) declared that the doctor's putation should not be at the mercy of every Tom k, and Harry who lodged a complaint against him H **Guy Dain** (Birmingham) however, replied that disciplinary machinery in the National Health rvice was as much protective as administrative n improved variety' of the regulations was on the nt of being put into operation.

RECLASSIFICATION OF CLOSED AREAS

he South West Wales division was concerned about reclassification of closed areas. Dr M J **Evans** said South West Wales had been closed for four or five rs and there had been no change in the conditions recently it had been declared an intermediate area W F **Dornan** (Sheffield) chairman of the Medical actices Committee said that the power to declare an s closed was given by a reluctant Parliament and an more reluctant Representative Body to see that st use was made of general practitioner man power It was never given for the purpose of protecting the interests of established practitioners Many areas under-doctored in 1948 had had an increase of 20% in the numbers of principals and one area, near South West Wales had had an increase of 300%, so that the relative position of South West Wales had altered.

OBSTETRIC LIST

In the discussion of this recurrent theme Dr J C. **Arthur** (Gateshead) said that obstetrics and gynæcology was a major subject in the medical curriculum like medicine and surgery and a doctor should be as free to practise the former as he was the latter Dr L H **Booth** (Hastings) took the view that with the ordinary qualifying degree a practitioner was not experienced enough for the emergencies of midwifery The chairman, Dr **Grant** remarked that the present policy of the association was that any practitioner should be entitled without question, to have his name on the obstetric list and Dr J S M **Ord** (Glasgow) reminded the meeting that this was the position in Scotland

PAYMENT OF COMPENSATION

Dr J W **McCarthy** (Hendon) asked the Representative Body to reaffirm its earlier decision that compensation for practices should be paid forthwith Dr D L S **Johnston** (Halifax) declared that it was the doctors money and the Government was getting it at a cheap rate of interest. The motion was carried and the meeting also asked that the rate of interest should be raised to an adequate level, that doctors wishing to incur capital expenditure on new or improved surgery premises should be able to obtain an advance payment and that a practitioner taking another into partnership should also receive a payment

OCCUPATIONAL HEALTH

Approval was given to new rates of remuneration for industrial medical officers which Dr J A L **Vaughan Jones** chairman of the occupational health committee, described as a considerable increase over the former scale and bearing comparison with those in other grades He hoped that ultimately the Government would implement the Gowers report

MEDICAL ETHICS

Dr **Robert Forbes** (Hendon) chairman of the central ethical committee, believed there was some danger that the ethical standards of the profession might be lowered He divided doctors into three kinds those who were always above suspicion in their relationships with other practitioners because that came naturally to them those who wavered, and the black sheep who needed herding to keep them in the fold Ethics would avail us nothing, he added unless they were directed to the benefit of our patients.

The meeting carried a motion from South Essex urging that, wherever practicable exchange of medical details concerning patients should take place only between doctors and deploring the increasing tendency to exchange confidential medical details direct with lay persons Dr R D **Milford** moving this motion said that in the early days a general practitioner made arrangements direct with a consultant with the increasing use of clerical staff in hospital the position had altered considerably He also had misgivings in relation to insurance

In the matter of the utterances of doctors in the press and on radio and television, Dr C P **Wallace** (Guildford) suggested that it was unwise to accustom the public to receiving medical advice from anonymous sources and it was a serious infringement of the freedom of professional men "It is important that we have the opportunity of declaring our views on medical matters, subject to the ethical code" Dr F A Belam (Guildford) pointed out that articles in *Family Doctor* were signed The public were entitled to the best, and doctors specially qualified were recognised as experts Dr Forbes said that a special committee had been set up to go into this matter

PUBLIC-HEALTH SERVICES AWARD

Dr J B Tilley, chairman of the public-health committee, declared that the award of the Industrial Court, referred to by Dr Gregg in his opening remarks, was of the gravest concern to the whole profession and to the whole of the public-health service In this he was reinforced by Dr Dain, who asked how there could be a preventive service if its condition were so bad that doctors would not enter it Most schools had stopped running D P H courses The public-health doctors had been "left behind," to the great danger of the public The meeting unanimously endorsed a motion from Gateshead that, in view of the dangers caused by the low levels of remuneration in the salaried medical services of the State and local authorities, steps should be taken urgently by the association to bring the remuneration to a level comparable to that of the rest of the profession in hospital and general practice

DANGERS OF DIESEL OIL

Dr J O M Rees (Guildford) asked the council to draw the attention of transport authorities to the possible dangers of fumes from diesel engines It would, he said, be a pity if London Transport's plan to replace the largest trolley-bus fleet in the world by diesel engined vehicles went too far without the authority being warned that this might not be in the interests of the public Dr Belam said Dr H B Howell of Bristol had attributed the incidence of carcinoma of the lung in sailors in engine-rooms during the late war to diesel fumes, and he had found carcinogenic deposits on the windscreen of his car in Bristol, a city which had a diesel transport fleet Dr A B Kettle (East Somerset) felt that, in view of the large number of vested interests concerned, only a body like the B.M.A could be effective The resolution was carried

ARBITRATION MACHINERY

Dr Gregg warned representatives that the question of arbitration machinery was not as simple as some imagined There must be fair arbitration, in which the association could have faith He repeated the council's words "After careful consideration of the whole position, the council is of opinion that the profession would be well advised to rely, for the present, on ad-hoc arbitration arrangements when disputes occur" Dr J L McCallum (Westminster and Holborn) asked the council to examine the possibility of getting some form of arbitration for the profession alone, and to this the meeting agreed

CRASH HELMETS

There was sharp criticism of the Government's action in refusing to exclude crash helmets from purchase-tax Dr J M C Gill (Aberdeen and Kincardine) was sceptical of the effectiveness of propaganda, but his suggestion for compulsion did not meet with approval The meeting, however, agreed with Greenwich and Deptford, and urged that all forms of protective clothing, including crash helmets, should be free of purchase-tax

Mr A Lawrence Abel (Marylebone) told of the delegation which went to the Board of Customs and [illegible] January The delegation pointed out that each [illegible] young men and women died on the roads of Britain and 18,000 were seriously injured, and a large number of these deaths and injuries would have been avoided if crash helmets had been compulsory The Customs and Excise officials told the delegation that no words of English could be conceived which could include crash helmets in the exemption from purchase tax of protective helmets worn by miners and quarrymen. "So we offered to send them a junior 16 year old clerk," Mr Abel added, as he opened fire on the authorities The tax people were getting 10*s* to 15*s* on each helmet, it was impossible to assess the value of the young lives lost, but the cost of the injuries was £4½ million—enough to run a hospital service in any one region There had been six months' delay since the delegation's visit, and nothing had been done, while hundreds of people had died on the roads If there was no improvement when purchase-tax was taken off, then let there be compulsion for wearing crash helmets

CONSULTANTS AND SPECIALISTS

Mr J R Nicholson Lailey deputised for Dr Rowland Hill, chairman of the Central Consultants and Specialists Committee, who was prevented by illness from attending the meeting Mr Nicholson Lailey admitted that the administration of the Joint Consultants and Specialists Committee might seem tedious, but warned that it would be a mistake to force a divorce between the Central Consultants and Specialists Committee of the B M A and the Colleges Nothing should be done which would enable the Government to negotiate separately or cause the consultants and specialists to set up their own organisation

Dr R P Liston (Tunbridge Wells) did not want the B M A to come to the hopeless position of the T U C in dealing with autonomous bodies, and Dr J A Pridham (Dorset) said that when the colleges cam down from their academic groves to the dusty are they had not the same experience as the B.M.A It w agreed that the council should review the relationsh of the Central Consultants and Specialists Committee the joint committee The council was also instructed consider the desirability of withdrawing from committe B of the Whitley Medical Council, "in view of the fa that this negotiating machinery is not work satisfactorily"

THE BAN ON HEROIN

Many speakers thought poorly of the ban on hero both for its effect and the way it was, imposed Dr J W Taylor (Aberdeen and Kincardine) declared "We are being denied the use of a most valuable dr for which there is no substitute We feel there was enough consultation with the general practitioners w are the greatest users of heroin" Dr Gregg said th the picture of heroin addiction presented to the standi medical advisory committee of the Central Health Servi Council was so dreadful that the sacrifice Britain wo make in not using heroin seemed small in compariso but he emphasised that he was not a member of th committee as a representative of the B M A It was mo regrettable that the B M A was not consulted and had no opportunity of circularising divisions to fo their opinion

Dr J S Happel (Winchester) asked "What of the other drugs of addiction? Where will the guillotine fal next?" Dr R Hale White (Marylebone) noted th in spite of the ban in other countries addiction there w increasing Dr John Noble (Blyth, Morpeth) remarke that the Government was giving pethidine to midwi and morphine to miners—and withholding heroin fro doctors Dr G E Moloney (Oxford) wanted to kno whether, because there were whisky addicts, whi manufacture was to be banned? (Cries of "No

And should the export of whisky be prohibited? ("Yes.")

Dr A. I MACLEOD (Outer Isles) however appealed to the profession to do without heroin in the interests of the world and Dr J G M HAMILTON (Edinburgh) said "We must regard ourselves as a responsible body—responsible not only to our patients and ourselves, but responsible internationally" Dr WAND deprecating parochial remarks, said the question was whether a few sufferers should be allowed a little extra suffering to try to solve a grave international problem

The meeting passed a resolution protesting against and asking for a reversal of the ban on the manufacture and use (but not the export) of heroin The resolution also pointed out that in the absence of consultation with the B.M.A. the Government could not claim to have consulted the medical profession

HOSPITAL MEDICAL STAFF

Mr NICHOLSON LAILEY announced that a claim had been made to restore the relative financial position of S.H.M.O.s. Dr E W, GOODWIN (Leicestershire and Rutland) said that consultants were overworked and registrars and S.H.M.O.s were doing the work of consultants. This could be overcome by increasing the consultant staff, which would also give incentive to hospital work. Introducing a motion from Dorset Dr PRIDHAM declared that house-officers were living near the poverty line Dr ANNIS GILLIE (Paddington) spoke for married women doctors, saying that they would like regular part-time hospital work which should not be of a "dead-end" type

HOSPITAL ADMINISTRATION

Criticising the Bradbeer report on the internal administration of hospitals, Dr V COTTON CORNWALL (Liverpool) saw in it interference from the lay secretary Dr L A GIBBONS (Reigate) said doctors were to be made the scapegoat of anything which went wrong in the hospital. Thousands of pounds were spent to convert a mansion into offices for little empire builders, while doctors were told to economise in dressings Dr A. KENE (Liverpool), referring to the Bradbeer recommendation for equal tripartite administration—medical, nursing, and lay—observed "The three members are equal partners, but the group secretary is twice as equal."

The meeting agreed with Liverpool that everything concerning the patient must be of importance to the clinician in charge and that therefore, lay and ancillary services must be subordinate to the medical so that equal tripartite administration was not in the interest of the patient Under no circumstances should the medical and nursing personnel be under the control of lay administrators.

STUDY LEAVE

Dr D S GREIG (Stirling) asked the Ministry and the Department of Health for Scotland to reinforce their instructions to regional hospital boards to make study leave available to hospital officers. Boards should be stimulated to provide locums where necessary one Ayrshire registrar had been waiting two years for study leave simply because he could not be spared

POLICY REAFFIRMED

On the last day of the meeting the Representative Body reaffirmed its policy on two points: by again expressing its strong opposition to a full time State salaried service and by stating that the Spens reports should still remain the basis in all negotiations on remuneration of doctors in every branch of the National Health Service

PREREGISTRATION POSTS

Dr ALICE GILBY (Westminster and Holborn) said that doctors in their preregistration year were getting a new 'slant' on the aphorism of Hippocrates "Art is long, Time is short, Judgment difficult, Opportunities fleeting" They complained that there were not enough preregistration posts in the larger hospitals they did not want to go away to the smaller ones for that prejudiced their chances later As it was difficult to dovetail posts, they might be faced with at least several weeks unemployment. Whitley committee B had not been able to find a means of giving them reasonable holidays The meeting asked the council to examine the situation and in view of the urgency to take immediate action in the light of their findings. Mr D S PRACY (Nuneaton and Tamworth) said that at present many listed preregistration posts were not suitable because there was insufficient supervision of the preregistration houseman by senior residents

POLITICS AND THE HEALTH SERVICE

The meeting declared that it was undesirable and detrimental to the interests of the health of the nation for the health service to be a means of gaining political capital, and that the service should be removed from the political arena. The motion was supported in two speeches which were not quite without political bias Dr J B W ROWE (Harrow) pointed out that at the last election one party had promised to abolish all charges and make a so-called free service whilst the other had said it would build more hospitals. It would be better to establish the service on a sound economic basis and administer it on non political lines. The present political interest, he thought was bad for mental health tending to make people introspective and neurotic Dr B HIRSH (Manchester) spoke of the 'fanfare of nauseating ballyhoo with which the service was introduced

TREASURER'S BADGE

Mr A M A MOORE, who retired as treasurer of the B.M.A. in 1954, presented a Treasurer's Badge to the association and invested his successor, Mr L DOUGAL CALLANDER.

Public Health

Salaries in the Public-health Service

COMMITTEE C of the Medical Whitley Council has accepted the Industrial Court's award on salaries of doctors in the public-health service[1] and has recommended all local authorities to put this into effect as from Jan 1 1955 The committee has issued a circular[2] containing detailed recommendations on salaries from that date.

Tuberculosis in Eire

The report[3] of the Department of Health for Eire for 1953–54 includes figures emphasising the remarkable change in the tuberculosis situation in Eire in the past few years The number of patients receiving treatment has steadily increased while the number of new cases coming under notice has decreased. The death rate has fallen steeply

Year	*No. of patients treated*	*No. of new cases under notice*	*Deaths*	*Death-rate per 100,000 population*
1949	25 050	7339	2717	91
1950	27 959	6706	2380	80
1951	30 338	6055	2162	73
1952	33 839	6705	1579	51
1953	36,03	6669	1190	40

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[1] Industrial Court award no 2563 See *Lancet* May 7 1955 p 961

[2] M.D.C circular no. 24

[3] To be purchased from the Government Publications Sale Office G.P.O. Arcade Dublin Pp 80 3s 6d

In England Now

A Running Commentary by Peripatetic Correspondents

WITH the railway strike the steel and coal may not be getting through, but the workers are And in London that is astonishing Leaving my home a dozen miles to the South I enter a line of traffic pelting along until half a mile short of the first roundabout There we stop, start, and stop again yard by yard until the roundabout is passed Then off we go to the next junction. Motorists have summoned hitherto unfathomed resources of patience never a hoot, and seldom a cut-in So have the non-motorists who wait good-naturedly at the bus-stops, or between the bus-stops hoping for a lift They start early and they may get there a bit late, but get there they do, and, remembering the frequent and crowded commuters' trains to the South that seems almost incredible. But if the general public has acquitted itself well, the police have done even better Working twelve-hour shifts, they have befriended us at every turn Parking the other day on the Embankment outside Scotland Yard I was approached by a constable Would I, he asked, mind going a bit further down? I went further down and saw him approaching almost at a run Trouble, I thought But no, he had come to ease me into a berth And so it has been all along

About the causes of our discomfort the people who have come in my car have been reserved Most of them have been more concerned about our stuttering economy than about their own uneasy journeys

* * *

A rail strike in full swing and a State of Emergency proclaimed Guy's simply had to be in on this!

We had bought a 1939 25-seater coach to convert to a caravan for our Continental holiday this summer Last week, with great effort, we removed the seats This week, with greater effort, we replaced them We obtained the permission of the Ministry of Transport to use this vehicle of unparalleled reliability and luxury, and dawn next morning saw us off Pulling up at our first stop, my conductor shouted his war-cry, "Purley, Croydon, Elephant, and London Bridge" Silence ensued among the surprised crowd, then the small voice of a schoolboy cried "Straight on, guv'nor, straight on!"

After this shattering start, we soon had a busful of passengers, who regarded us with obvious misgivings but settled in their seats or allotted standing-room with commendable resignation Extracting our fares, we were surprised to learn that other pirates had been on the road before us and were charging even more Imagine our fury at undercutting our allies and patriotic colleagues!

Streatham Hill, a full load of 6 tons, and a warm day spelt disaster to the old bus She coughed, choked, and stopped We lifted the bonnet and applied a universal remedy with this bus—blowing down the petrol feed with a bicycle pump Rewarded by the petrol cap flying off the tank, we replaced the bits and climbed in Surprisingly, the engine started, and again we staggered along

We soon learned the language of our adopted calling as, asphyxiated by carbon monoxide and boiled by the heat of the engine, we threaded our way through the packed traffic The final right turn into London Bridge Approach, with Austin 7s under the bonnet and cyclists under each mudguard, was as exciting and dangerous a piece of busmanship as any After nearly two hours of their unwilling company, we dropped our passengers To our astonishment, some seemed genuinely grateful and one or two even asked what time we were running that evening

One disappointing feature about our first week as rivals to the London Transport Executive was that we made just 7s profit But maybe, by the Executive's standards, that's good going!

* * *

"Harley Street Doctor," who contributes to one of the evening papers, has been advising his readers on how they [illegible] "perfect patients"—from his point of view [illegible] be objective, honest and accurate in describing [illegible]oms" Yet they "should avoid volubility"

"It will be helpful if the patient has a good *general* idea of how the body works" But "few people are more difficult to handle than those who think they know *more than the* doctor in both diagnosis and treatment"

In response to the question how long has a symptom been present, the doctor "will not be satisfied with the reply 'a long time' He will want to know how many days weeks, months." (Does he really expect such information? I have more than once encountered patients who have completely forgotten an extensive laparotomy until their attention was directed to a long abdominal scar) And also "if the symptoms are getting better or worse, are continuous or intermittent And what relieves or aggravates them?"

"In mentioning previous illnesses, don't ignore any because they appear to be too trivial"

No, dear "Harley Street" colleague, it is not the patient's obligation to distinguish irrelevancies from essentials, trivialities from matters of importance Nor can one expect it He is likely to be scrupulously accurate about the weight of the case of bananas that fell on his foot, and to consider as of the greatest importance the number of the motor-car that knocked him down (which indeed it well may be to him, with his eye upon compensation, or to the police with the prospect of legal proceedings) I once had a frantic telephone message at 3 A.M from a highly educated man, unable to sleep through the pricking of conscience, recalling that during our consultation he had informed me that he was 56 years old whereas he would not reach that age until the end of the following week For all he knew, such a detail might be of profound significance in my understanding and treatment of his complaint

As an elder (perhaps not better) soldier, I feel disposed to suggest to the writer that the core of the matter is not the education of his prospective patients but the *continuous* education of himself To obtain the necessary coöperation is the doctor's business the adjustment to get en rapport naturally varies with the individual, and the really good doctor converts every patient into a "perfect patient" That surely is the art of medicine.

* * *

My quince is in full bloom, if ever a quince is in full bloom It always reminds me of chickenpox, for it flowers seem to come out in a series of crops When I went away on Wednesday, May 25, there were a few buds, and when I returned on the Saturday these were in full flower, of the colour of typhoid spots, which resemble the tint best illustrated by the English unofficial rose Besides the flowers already out, there are now many more buds, which I expect will burst forth on Sunday, Monday, and Tuesday, for some are tight and others loose It is unwise to count one's quinces be they have matured, but my two trees have in the often produced a marketable surplus I wonder whe the quince in Crete, which the O E D suggests is natural habitat, has sweeter fruit than our own

* * *

At last I have been to a Roses match at Old Traff With plenty of cricketing characters on both si there was little danger of boredom, and what be than the moment when Statham was called upon prevent—and only just, by jove—a hat-trick by Yorkshire rival, Trueman As the match fluctua excitingly, the steady stream of evening newspapers w one move behind "Lancs steady start" we read con ingly as the middle batsmen failed, but, safe in knowledge that the tail was wagging before our v eyes, the headline "Lancs slump" did not worr It was only when we came to read our pink or gre sports specials on the way home that we realised full glory of the day's proceedings, not only had important Yorkshire wickets fallen in the last minutes of play, but first-class cricket had been rain off nearly everywhere except Old Trafford Now th really is something to make a Mancunian holiday!

* * *

Overheard in outpatients

"What is your job?"

"*I work a Hollerith machine for the* C W.S"

"And what do the C W S use a Hollerith machine for?"

"For punching holes in cards"

Letters to the Editor

CIVIL SERVICE MEDICAL APPOINTMENTS

SIR,—The secretary of the Civil Service Commission is surely all too ingenuous in his reply last week to "Toad Beneath the Harrow" What he has done is to seize on a few words in the Toad's letter and avoid replying to the main point of it.

The point is that in the document issued by the Civil Service to applicants for appointment as medical officers on p 10 under the heading of prospects, it says that higher posts in the medical officer class are normally filled by promotion from the grade of medical officer and then goes on to refer to 14 posts above the grade of principal medical officer This, as the secretary of the commission must know is not a statement of fact. As the Institution of Professional Civil Servants pointed out in the evidence that it submitted recently to the Royal Commission on the Civil Service

> "One of the standing grievances of the medical officer class is that to an extent unknown in any other Civil Service class higher posts are filled by direct recruitment instead of by promotion. It is a fact that in the appointments since the end of the war not one of the chiefs other than the principal medical officer acting as chief in the Ministry of Fuel and Power has served as a basic grade medical officer in the Civil Service These chiefs and some of the deputies and indeed some of the principal medical officers, have been drawn from outside the Civil Service It is a serious reflection on the administration of the medical Civil Service that there is this constant bringing in of officers from outside for it causes intense dissatisfaction and frustration among the highly competent staff with many years of efficient service to their credit"

There is also an interesting comparison to be made between the administrative class in the Civil Service and the medical officer class. In the medical Civil Service out of a total of some 506 officers, temporary and established, there are only 135 above the level of the basic grade: that is to say on the face of it, a one in four chance of promotion For the 703 assistant secretaries in the administrative class in the Civil Service, there are no fewer than 310 higher posts that is to say a one in two chance The practice is, however vastly different In the medical officer class the position is as described in the previous paragraph

In the administrative class it is most exceptional for any post in the higher levels to be filled other than by promotion

While these facts remain as they are the Civil Service Commission ought to be more careful in its statements to prospective recruits to the Civil Service, unless it wishes to be accused of dishonesty

Institution of Professional
Civil Servants
Queen Anne's Chambers
28 Broadway London, S W 1

STANLEY MAYNE
General Secretary

QUARANTINE MEASURES IN POLIOMYELITIS

SIR,—The article by Dr Goffe and Miss Parfitt in your issue of June 4 will arouse widespread comment and is of the greatest interest

There are of course two schools of thought on the spread of poliomyelitis. There is the "narrow stream" concept of Dr W H Bradley of the Ministry of Health and there is the concept propounded by Dr F O MacCallum director of the Virus Reference Laboratory Colindale The latter concept is based on studies of the presence of the virus in sewage and favours a broad stream—the "epidemic" property of the virus concerned determining whether an epidemic shall occur

Most medical officers of health acting on the former view make the recommendations favoured by the W H O expert committee and used apparently without success in the epidemic investigated by Goffe and Parfitt The fact that a few contacts may excrete the virus in the stools for longer than 21 days will not invalidate this period for me until investigations on a much larger scale are carried out Dr Bradley in his paper at Scarborough in 1953 drew comparisons with scarlet fever and diphtheria and said "Epidemiologists have long since learnt that although corynebacteria and streptococci are extremely widespread in nature strains capable of hurting man spread locally giving rise to discrete outbreaks" So in this respect, both the epidemiology of the Ministry and the virology of Colindale are in agreement.

Personally I believe the only answer is in widespread immunisation which has assisted the natural disappearance of diseases such as diphtheria and yellow fever in human beings, and distemper and hard pad in dogs. Until this day arrives, isolation of cases and quarantine of contacts must be the measures to be followed.

But splendid investigations such as the ones you have published are in line with the W H O recommendation for further study of the practicability and effectiveness of isolation and quarantine as applied to first families in a community in the control of poliomyelitis.

Public Health Department,
Beckenham, Kent

L R. L EDWARDS
Medical Officer of Health.

TREATMENT OF CHRONIC AMŒBIC DYSENTERY

SIR,—In your issue of March 26 Dr Andrade reproves Lieut Colonel Inder Singh for stating that emetine will control acute amœbic dysentery, but that the *amœbic cysts are not affected* Dr Andrade suggests that it is irrational to suppose that the finding of harmless cysts provides any information other than that they must have originated from trophozoites He implies with obvious reason that an egg must have been laid by a pre-existing hen and that the only rational treatment is to attack the hen not the egg But he goes further and states that the presence of cysts is merely indicative of an infection of the bowel *wall* with amœbæ. There is a good deal of evidence that this is not so and that the presence of cysts indicates rather strongly that the pre existent trophozoites are living in the *lumen* of the bowel.

This theory has been reintroduced by Hoare and has much to recommend it in explaining the relationship of infestation to morbidity in amœbiasis This theory of intraluminal symbiosis carries also a lesson in therapeutics.

It is well known that

(1) Patients with the dysenteric form of amœbiasis pass trophozoites not cysts.

(2) In asymptomatic and mildly symptomatic amœbiasis cysts are very often passed and trophozoites are often not seen

Recently we have shown that certain drugs can convert the trophozoite passing patient into the asymptomatic cyst passer and these findings will be published shortly

> *We believe that these observations support Hoare s* contention that amœbæ can live free in the bowel and that when they do so they achieve the ultimate design of their existence and reproduce themselves by cyst formation as Nature intended Their intraluminal habitat does not necessarily imply that they live *only* in the middle of the bowel contents. If they did it might be presumed that only a dose of Epsom salts would be needed for complete eradication It may be reasonably contended that they live in the contents of the crypts but essentially they do not invade the tissues We believe therefore that the passage of trophozoites is evidence of invasion, of ulceration and of true pathogenicity: and that the passage of cysts is evidence of lack of invasion and ulceration and in favour of the amœbæ living harmlessly as commensals in the lumen of the bowel

If this is true, Colonel Inder Singh s *observation* (and indeed that of many other observers) that emetine does not eradicate cysts is easily explained For a systemic amœbicide acting on the tissues by virtue of its being carried by the blood, would not be expected to destroy either cysts or their antecedent amœbæ in the lumen of the bowel

We feel that when patients are found to be passing cysts they *must* be treated with intraluminal amœbicides —e g , the antibiotics and diodoquin For extra security it is sensible to add a harmless systemic amœbicide such as chloroquine In dysenteric amœbiasis the systemic amœbicides, emetine or chloroquine, are mandatory as well as the intraluminal amœbicides

We believe the finding of cysts indicates the presence of the intraluminal phase, but the finding of trophozoites, apart from possible hæmatophagy, does not distinguish between the two possible phases Thus, the differential finding of cysts or of trophozoites has a considerable significance in treatment and prognosis We consider that much of the controversy over the results of the many modern treatments reported in the last few years, is due to failure to appreciate the differences between the intraluminal and invasive phases of amœbiasis

Amœbiasis Research Unit,
South African Council for
Scientific and Industrial
Research, Durban

T G ARMSTRONG
A J WILMOT
R ELSDON-DEW

SIR,—Lieut -Colonel Inder Singh displays another common misconception, in his letter of May 28, when he says that " unless both cysts and amœbæ are destroyed, some of the cysts may develop into amœbæ before they are excreted and thus restart the infection "

In kittens, acute *infection* can be readily produced by rectal injection of material containing cysts of *Entamœba histolytica*, but in man the cysts do not undergo any further development in the intestine and, once formed in the lumen of the bowel, do not excyst again in the same host The cysts, therefore, are not parasitic and are harmless to the host in whose bowel they are formed They are, of course, infective when swallowed by a new host

It is customary to use a combination of drugs in the treatment of amœbiasis not because it is necessary to kill amœbæ *and cysts*, as is suggested by Colonel Inder Singh, but because amœbæ live on the mucosal surface of the large bowel and within its lumen and also penetrate into the mucosa and submucosa, thus necessitating the combined use of an amœbicide which acts locally in the gut and one which exerts its action after absorption

I repeat that cyst destruction forms no part of the aim of treatment and, in support, may I quote Dr A R D Adams,[1] of the Liverpool School of Tropical Medicine

> " It follows therefore that any treatment given to eradicate the infection of the large bowel must be *directed against the* amœbæ there, and it is quite pointless to consider treatment to destroy the harmless inert cysts which form in the stools, their presence there being merely indicative of the presence of an infection with amœbæ This matter is one of importance and is worthy of stress in view of some statements in the literature in relation to the drug treatment of intestinal amœbiasis These statements assert that one drug is given to *destroy the amœbæ* and another to destroy the cysts, it having been observed that the drug destroys the latter in vitro It is by no means certain that any drug given by mouth destroys cysts *within the lumen of the gut* , it is much more probable that the parent amœbæ would be destroyed by such a drug, and that it is their destruction which accounts for the disappearance of the cysts from the stools No treatment at all is necessary to destroy the cysts , and indeed, if it were possible purposively to do so their destruction would have no influence on the parent infection When the treatment is stopped, further cysts would immediately reappear in the stools so long as the parent infection remained "

Calcutta.

C B ANDRADE

CANCER

SIR,—I write to disagree with Dr Hazel Baker (May 21), for I fear that she is arguing from the particular to the general

Because one surgeon surprisingly insisted on having an exploratory laparotomy for (as he was assured) non-existent carcinoma, there is no reason why the public should not be made aware of two important facts. These are (1) the varied symptoms of cancer , and (2) that if these symptoms are reported without delay to their doctor there is every chance of a cure, and not necessarily by the knife

Many will admit that there is nothing more alarming than poliomyelitis, and yet look at the enormous amount of publicity its symptoms have received in the press and through the B B C —and most valuable publicity in *my view insomuch that* parents and others now are amply warned

I would like to see equal publicity given to cancer symptoms There will always be the nervous person too frightened to do anything about it, but there may be hundreds of others—luckily more courageous—who would take advantage of this knowledge and *promptly* enlist medical advice to prove or disprove their suspicions.

I write not as a member of the medical profession—though married to one—but as one who lost a very near and dear relative who died of cancer because he was too late in asking for medical advice—not through fear but through ignorance

Woodhall Spa,
Lincs

LILY BOYS

RENAL SHUNT IN SHOCK

SIR,—A large number of experimental studies on the renal circulation in shock have been undertaken, but comparatively few observations on human beings have so *far* been published The *following observations* may therefore be of interest

A patient, aged 28, with aortic coarctation and hypertension, was subjected to renal-vein catheterisation At 13 hr 30 min hyposulphite and *p* aminohippurate (P A H) clearances were started, causing *some vomiting* They gave the following results

C_{Hypo}	C_{PAH}	Blood flow	Filtration fraction	E_{PAH}	Blood pressure (arm)
140	469	610	0 18	100 %	180/100

At 16 hr 20 min , under radiographic control, *the catheter* was seen in place in the renal vein and the venous pressure was 6 5 mm Hg Maximum P A H extraction was obtained Oxygen and bicarbonate levels in the renal venous blood were within the normal range

At 16 hr 30 min the patient showed all the clinical signs of shock and the blood-pressure of the upper limbs fell to 120/60 At this moment blood from the femoral *artery and renal vein was obtained* and the amount of O_2, CO_2H, Na, and K was estimated The following were the figures obtained

—	Oxygen		CO_2H		Na		K		Venous pressure
	Artery	Vein	Artery	Vein	Artery	Vein	Artery	Vein	
Before shock	?	10 06	?	40 50	?	?	?	?	6 5 mm. Hg
During shock	11	11 44	47 04	47 64	130	139	3 7	4 3	0

About 5 minutes afterwards all the signs of shock increased and no more blood was obtainable by aspiration through the catheter *As radiography* confirmed that the catheter was well placed in the renal vein, it was evident that no blood was circulating through the kidney at this stage Saline *solution injected* by the catheter was reaspirated without blood Thus the renal circulation had completely ceased Shortly after the removal of the catheter the patient recovered from shock.

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[1] *Practitioner*, 1952 168, 419

We have no knowledge of the oxygen content of the arterial blood of this patient before shock but we have no reason to assume it was not normal The oxygen of the venous blood both in the right auricle (8 51) and in the renal vein was normal The sudden and sharp ue of the venous oxygen and bicarbonates during hock can be explained only by a striking readjustment of the renal circulation during shock The following ratio serves to explain the exclusion of the functional renal tissue in shock when the circulation through the kidney is maintained

$$\frac{\text{Renal arteriovenous difference in } CO_2 \times \text{ blood flow}}{\text{Renal arteriovenous difference in } O_2 \times \text{ blood flow}}$$

No other explanation seems possible than the presence in the human kidney under conditions of shock, of a shunt such as that described by Trueta and his associates —an arrangement whose existence in man has been doubted.

The complete suppression of the blood flow through the renal vein at the more severe stages of shock seems to accord with Van Slyke's concept of the sacrifice of the renal circulation We are not in a position to explain the levels of extraction of Na and K but we must remark that the latter appeared in a slightly higher concentration in the blood of the renal vein as if K had been liberated by the anoxic tubular cells

In this case we were not able to detect spurting of the renal venous blood, but in another patient under shock spurting was noted In this case the arteriovenous oxygen difference was normal.

Department of Clinical Medicine
Hôpital Purpan, Toulouse

P MÉRIEL
F GALINIER
J M SUC
M. DESANDRE.

A BARBITURATE ANTAGONIST

SIR,—When one of us (F H S) replied to Dr McElligott (April 16) the excellent article of Dr Wright [1] was not available for perusal. However the statement (May 7) that little barbiturate would remain in the body after six days was not a generality but was based on the experience of one of us (N E W McC) who has been studying barbiturate metabolism for some years past

Dr Wright has found that phenobarbitone disappears from the plasma at the rate of 15% per day and calculates that after the ingestion of 72 grains of the compound, there would be 27 grains present at the end of six days. This calculation appears to imply that phenobarbitone is removed from the body solely by renal excretion whereas it has been established that some % of administered phenobarbitone cannot be recovered from the urine

In one of our patients who was known to have ingested at least 100 grains of phenobarbitone traces of compounds showing a *spectrophotometric absorption similar* to barbiturate absorption were present in serum and urine eight days later We have however spectrophotometric and other evidence which strongly suggests that phenobarbitone was not the only compound which is contributing to the absorption This evidence was supported in experiments with dogs

As we have said it has been established that only some % of ingested phenobarbitone is excreted as such in the urine [2] The larger proportion is metabolised in some unknown fashion but from what we know of the destruction of other barbiturates it is likely that the ring structure remains intact at first We also have evidence that at least one of the possible decomposition products of phenobarbitone has an absorption similar to that of the parent substance In view of the fact of such destruction *of phenobarbitone in the body I would suggest that* some of the material estimated spectrophotometrically by Dr Wright [1] is of metabolic origin In other words in the absence of detailed knowledge of phenobarbitone metabolism the results of analyses obtained by spectrophotometric methods should be interpreted with caution

Also we do not agree that the worth of new barbiturate antagonists can be evaluated by a measurement of drug levels in the blood The only test is the pragmatic one of a lessening of the duration of coma and the mortality rate. The suggestion that barbiturate intoxication is best treated by conservative methods will be the subject of another paper

University of Melbourne
Australia

F H SHAW
N E W MCCALLUM

ELECTRIC BLANKETS

SIR,—The attention of the Standing Interdepartmental Committee on Accidents in the Home of which I am Chairman has been drawn to the letter by Dr Maddison in your issue of April 16 giving directions for making an electric blanket The committee think it desirable that your readers should be warned that blankets of this kind may be dangerous unless certain precautions are taken which Dr Maddison would no doubt have wished to mention had space permitted These include the incorporation of thermostats and secondary fuses as a protection against overheating and the use of a transformer embodying a safeguard against a fault developing between the primary and secondary windings which would otherwise have the effect of making the blanket live at mains voltage

In addition it should be borne in mind that the repeated folding of conductors of the type suggested would in time cause deterioration of the insulation and breaking of the conductors themselves giving rise to risk of burns and shock

Since considerable technical experience is necessary to make the above precautions effective it may be unwise for anyone without proper qualifications to attempt the construction of an article which requires highly specialised knowledge for its successful production

Home Office,
London S.W 1

AUSTIN STRUTT

DIURESIS FROM CARBONIC ANHYDRASE INHIBITION

SIR,—Your leader of April 2 was remarkable in its scope and balance and certainly represents the best available statement in this complex and controversial field. May I be permitted a few comments on several of the technical questions raised ?

(1) The maximal *rate* of HCO_3^- excretion following acetazoleamide ("Diamox") may show a logarithmic relation to dose but this is only in the range 0·1 mg per kg to 5 0 mg per kg [3,4] Above this range and at clinical levels the dose-response curve is flat; *there is little difference between HCO_3^- excretion rates* following 5 or 100 mg per kg orally [4] This suggests that inhibition of renal carbonic anhydrase is essentially complete at the therapeutic dose range of 5–10 mg per kg The *total* amount of bicarbonate excreted after a single dose however is a function of dose in the 5–100 mg per kg range since the dose determines the duration and hence the final magnitude of effect

(2) The diuretic effect of acetazoleamide is *not* necessarily dependent on plasma HCO_3^- concentration in the range 12–22 m eq per litre Lowering of *plasma* HCO_3^- by hyperventilation or by a moderate single dose of acetazoleamide itself does not block the renal response since in these situations

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[1] Wright, J T Quart J Med 1955 24 9

[2] Maynert, E. W., van Dyke H B *Pharmacol Rev* 1949 1 217

[3] Counihan T B., Evans B M Milne M. D *Clin Sci* 1954 13 583

[4] Maren T H., Wadsworth B C, Yale E K, Alonso L G *Bull Johns Hopk Hosp* 1954 95 277

comparatively little "buffer base" is lost, it appears that it is the *total* quantity of base lost or net body acidosis that prevents the renal effect Such acidosis is achieved on continued administration of drug but is imperfectly reflected, in quantitative terms, by plasma HCO_3^- concentration [4]

(3) There is no doubt that opinions on the diuretic effectiveness of this drug "vary from virtual nihilism to considerable enthusiasm" But in the nihilistic paper [3] no patients were treated for more than one day, and in the enthusiastic papers there were no controls in whom diuretic therapy was withheld [5,6] Certainly it should be possible to chart a course between these extremes You foster one notion that has led some to nihilism—the idea that there must be chloride loss to relieve œdema But until the careful documentation that you call for has been made, it will be well to reserve judgment on this point

(4) Excretion of potassium in cardiac patients otherwise resistant to acetazoleamide has not generally been large On the first day of drug the K^+ output does not appear to exceed greatly the daily intake,[3] and output diminishes strikingly on the second and third day (as it does in the normal) even with continued drug administration [7]

(5) Of your several searching questions, we may suggest an answer to one That hyperchloræmia persists during long term acetazoleamide treatment is not surprising, in view of the fact that the metabolic acidosis persists as long as the drug continues For although urinary acidity and ammonia return to normal, they do not (in the presence of the drug) *exceed* normal, and thus the initial base deficit is not repaired Chloride may be regarded as a "filler" to bring the anion level of plasma to normal in the face of low plasma HCO_3^-

Experimental Therapeutics Section,
American Cyanamid Company,
Stamford, Connecticut

THOMAS H MAREN

TEACHING DEAF CHILDREN

SIR,—We know of several deaf children whose parents were told by E N T specialists that there was no urgent need for special school training until the children were five As the majority of doctors know, the 1944 Education Act says that all handicapped children should begin their education at two, and it is only because there are not sufficient school places available at present that this section of the Act is not being fully implemented

We find that children who begin school at four or five years are educationally very backward, compared with those who begin at two, particularly with speech training and language development The task of any teacher of the deaf is made infinitely more difficult when the child starts school late I think I can say that this is the unanimous view of all teachers of the deaf

It is therefore a disservice to the child and disappointing to the teachers to know there are still specialists who have not caught up with the 1944 Act

Nursery School for Deaf Children
Woodford Green Essex

B I INGALL
Principal

CHINESE MEDICINE

SIR,—I was very interested to read Dr James's article in your issue of May 21

Chen Chiu therapy or, as it is generally known in Europe, acupuncture has now a very wide following in France owing chiefly to the work of M Soulie de Morant, who was French Consul in China for some twenty years He was so impressed by the results which he saw of acupuncture that he studied it and went through the Chinese hospitals, and now has trained many doctors *in France* M Soulie de Morant died recently

I can speak from personal experience of its efficacy in many cases—in hæmorrhoids and in improving hearing due to adhesions of the eustachian tubes, for instance What impressed me most about this system was the method of diagnosis It is not necessary to tell an expert practitioner what is wrong with you he tells you!

While I was with M Soulie de Morant a lady came in suffering from very acute irritability He felt the pulses (there are supposed to be five or more pulses in each wrist, each corresponding to a different organ whereby they can tell the health of that organ) and he immediately remarked to the lady "I am not surprised Both your liver and spleen are enlarged and are pressing on the internal organs" He applied two needles and the result was almost instantaneous All the drag underneath the eyes disappeared and the result, I believe, has been lasting

M Soulie de Morant has written several treatises on acupuncture, and the work which he did is being carried on by many enthusiastic students

I have never been able to explain how the method works but it does work, and it certainly is capable of reducing hypertension

London, W 1

HERBERT A BERENS

STAPHYLOCOCCAL INFECTION IN THE NEWBORN

SIR,—The proper use of antibiotics is such an important issue for contemporary medicine that we hope that you will allow this friendly Border fray to continue for a little longer We should like to comment on three points raised by Dr Forfar and his colleagues in their letter of May 21

(1) On the question of the interpretation of their original article (March 19), we must plead guilty to the charge of having failed to qualify the term "infection" with the adjective "staphylococcal" throughout our letter the reason being that we were quoting almost directly from their article at the point where, under the subheading *Present Investigation,* they stated that "In Hospital E all clinical infections were treated with oral erythromycin In Hospital W clinical infections were *treated with the same dosage of erythromycin at the* same intervals" They also stated specifically that all cases of conjunctivitis were treated in the first instance with systemic erythromycin, and with local chloramphenicol only when this form of treatment failed They did later state, under *Discussion,* that "In most c of conjunctivitis systemic therapy is not indicat but this view was not repeated in the summary an seemed less consistent with their expressed objec preventing the development of serious sepsis, for w purpose a systemic antibiotic would appear to be n *rational Our own experience, of course,* has led u reject the routine use of any antibiotic in this prop lactic manner (as described in your issue of May 7)

(2) On the question of the relative merits *of ch* amphenicol and sulphacetamide drops in the rou treatment of conjunctivitis, we feel that an import point of general principle has been raised Leaving a the question of the doubtful value of in-vitro testing sensitivity to sulphonamides, we prefer to use sul acetamide to treat this relatively trivial form of infect because we know that at the present time no patie life, *threatened* by severe staphylococcal sepsis, depe upon his organism being sensitive to a sulphonam drug there are more potent drugs available, and ch amphenicol and erythromycin *are two* of them therefore feel it of the utmost importance to rese such drugs for potentially fatal infections It might fact be profitable to try out older and *simpler reme* again, such as normal-saline eye-drops

(3) On the question of the risk that babies who home with an unresolved clinical infection may spre resistant strains of staphylococci to the community, would only say that the problem is a much bigger than Dr Forfar and his colleagues suggest Numero studies have shown that up to 85% of normal babies *maternity* hospitals are carrying staphylococci of hosp strains in their noses, cord stumps, or conjunctival s by the end of the first week of life (we need only quo *the figure* published by Dr *Forfar* and his colleague their article of March 19, that staphylococci we recovered from 76% of the umbilical swabs taken) T carry their argument to its logical conclusion, they wou have to treat all these babies, and not only those w were clinically infected

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[5] Bolsky H *New Engl J Med* 1953 249, 140
[6] Ruskin A *Arch intern Med* 1955 95, 24
[7] Leaf A Schwartz, W B, Relman W B *New Engl J Med* 759

We believe that at the present time the use of the more powerful antibiotics should be restricted to the minimum. If we cannot prevent the babies taking staphylococci home with them we can at least try to reduce the risk of their organisms being resistant to the drugs on which their lives and those of their household contacts may later depend

S D M COURT
C A GREEN
J G P HUTCHISON
G A. NELIGAN

Princess Mary Maternity Hospital
Newcastle upon Tyne

HEROIN

SIR—The Government have decided that supplies of heroin shall be withdrawn at the end of the year All practitioners realise the dangers of addiction to this drug but surely the addict obtains his supplies from different sources ?

There are three dangers in this legislation

(1) The profession will be deprived of a powerful drug which has a definite place in both medical and surgical treatment

(2) It will no longer be possible to treat established addicts with decreasing doses of heroin.

(3) Practitioners who use this drug will be tempted to buy a large quantity of heroin before Dec 31 for their future use.

This is the first occasion that it has been necessary to prohibit the use of a drug Surely the amount of addiction in this country does not warrant such a severe measure ?

W F W SOUTHWOOD

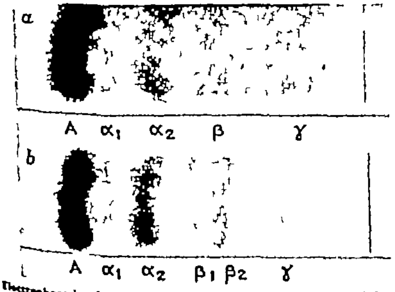
West London Hospital
London W 6

⁎⁎⁎ As was explained at the representative meeting of the British Medical Association reported on p 1218 the ban is being imposed by this country as part of an international effort to prevent heroin addiction We should prejudice the success of this effort if we dissociated ourselves from it —ED L

ELECTROPHORESIS OF PLASMA-PROTEINS

SIR,—In his letter of April 23 Dr Owen reported that under certain circumstances using a Veronal buffer for paper electrophoresis he has obtained a separation of the β globulin into two components This is contrary to the usual experience also shared by us that β-globulins travel as a single band in such systems when no other ions are added

We have found recently however that in some patients (see accompanying figure) heparin causes a splitting of the β-globulin band This phenomenon has been observed only when heparin was injected in the fasting state and hitherto we have found it only in sera from patients with severe diabetic angiopathy and the Kimmelstiel Wilson syndrome When heparin was given after a fatty meal no separation of β globulins occurred, and no separation was observed in post heparin sera from patients with recent diabetes mellitus or from non-diabetic patients with chronic kidney diseases



Electrophoresis of serum (a) before and (b) after heparin injection.

H V LAUTRUP CHRISTIANSEN

Kommunehospitalet,
Aarhus, Denmark.

THE DEPARTMENT OF PHYSICAL MEDICINE

SIR,—I was very interested to read the report (May 28) of the annual meeting of the British Association of Physical Medicine.

It is a deplorable fact that at present patients can be treated only in central departments of physical medicine because only there could be found the requisite medical and technical staff and equipment.' This entails much loss of time in travelling and waiting by patients

At the inception of the National Health Service various alternatives were offered to the Minister of Health for setting up peripheral clinics staffed by qualified physiotherapists to avoid the anticipated difficulty of waiting lists, expensive hospital transport and harassed physiotherapists. The Minister saw fit to rebuff all these efforts Dr Fell it seems did not specify whose brains should be pooled to solve these problems.

Dr Cooksey voiced the concern of many at the shortage of physiotherapists May I point out one reason for lack of recruitment ? Parents see little advantage in educating their children at university level for three years when the eventual remuneration just does not compare with other professions and occupations.

LEONORA MASON

Bristol 4

PROLONGED JAUNDICE

SIR,—I read with interest the paper by Dr Klajman and Dr Efrati in your issue of March 12 They refer to the condition described by Dubin and Johnson [1] and in their summary they emphasise that clinical examination revealed nothing abnormal except jaundice and slight enlargement of the liver

I would like to draw attention to a similar if not the same disease (or perhaps I should say condition) described in 1948 by Rotor Manahan and Florentin [2] In their cases the van den Bergh reaction was directly positive, and the blood bilirubin showed a considerable increase in hepatic or crystalloid bilirubin but there were no symptoms of obstructive jaundice the urine did not contain bile and the stools were normal in colour

I had the chance to observe the children of one of the families in this series In my paper [3] I said that the syndrome was marked by jaundice the accumulation of hepatic crystalloid bilirubin in the body and the absence of occlusion of the biliary passages or any other liver damage It was congenital and familial Although the first signs could be observed in early infancy it seemed that the jaundice became latent during infancy for some unknown reason but manifested itself again later and persisted throughout life The ætiology was completely unknown The liver disturbance was confined to bile metabolism

It has been said that this kind of jaundice is quite different from the familial non hæmolytic jaundice described by Dameshek and Singer in 1941 [4] I believe that the condition described by Dubin and Johnson and by Dr Klajman and Dr Efrati are similar if not identical and I wonder whether the disease really is a new clinico pathologic entity if it is in fact due to an inborn error of metabolism In that case one would expect the condition to be *familial and inherited* as we found it to

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1 Dubin I N Johnson F B *Medicine, Baltimore* 1954 33 155
2 Rotor A B Manahan L Florentin A A. *Acta med philipp* 1948 5 37
3. Stransky E *Ann pædiat* 1950 175 301
4 Dameshek W Singer K *Arch intern Med* 1941 67 259

be As in the case described by Dr Klajman and Dr Efrati, in our cases the gall-bladder did not fill with opaque dye and the patients were in excellent health

Department of Pædiatrics, College of Medicine, University of the Philippines Manila — EUGENE STRANSKY

ENURESIS

SIR,—Following the recent correspondence, I wish to cite the following case, treated at the Liverpool Royal Infirmary, which seems to fall into the category of “ acquired relative nocturnal polyuria ” [1]

A youth of 20, an only child, was said to have first had nocturnal enuresis at the age of 10 He was referred to the psychiatric outpatient clinic after being fully investigated physically and “ having had every treatment except hypnosis ” He was accordingly treated by hypnosis and suggestion for some months but his condition showed only slight improvement During the past few months he has been treated with posterior lobe pituitary snuff (‘ Disipidin ’), as advocated by Hansen,[2] and improvement has been marked

The initial dose was gr 1 (60 mg) at night and this gave an immediate good result Five weeks later, without the patient’s knowledge, an inert snuff was substituted, and this was followed by a complete relapse Disipidin was restarted at gr 1½ (90 mg) at night and later increased to gr 2 (120 mg) The accompanying table illustrates the results

DRY AND WET NIGHTS PER TWO WEEK PERIOD DURING TREATMENT WITH DISIPIDIN

Wet	4	7	9	3	3	5	4	1	0	3	2	0	0
Dry	10	7	5	11	11	9	10	13	14	11	12	14	14
	Disipidin (gr 1)		A	(gr 1½)	Disipidin (gr 2)								

A = inert powder for last seven days of this fortnight Six of these nights were wet

Dr Poulton (March 19) points out that it is possible by bladder training alone to achieve control, even in the case of a patient excreting equal volumes by day and night, but goes on to say “ in general, ancillary aid must be brought to bear ”

The case I have described suggests that posterior-pituitary snuff, by increasing absorption by the epithelium of the renal tubules, might have a useful place in the treatment of cases classifiable as absolute polyuria and relative nocturnal polyuria

Rainhill Hospital, near Liverpool — MICHAEL J COSGRAVE

STERILISATION OF SYRINGES

SIR,—In your annotation of Jan 22 you state that “ autoclaving is unsatisfactory because the syringes have first to be taken apart ” This was challenged by one of us (W N R) in your issue of Feb 19, and in their reply of March 5 Dr Darmady and Dr Hughes state “ If Dr Rollason likes to carry out the simple experiment of placing dried spores in the bottom of the barrel with the plunger in position he will soon be convinced that autoclaving under these conditions is not desirable as a method ” Such an experiment has now been carried out by one of us (J G A) using the autoclaves in many of the hospitals in this area

The spores used were the same as those used by Dr Darmady and Dr Hughes—namely, those contained in “ green label ” earth as kindly supplied by Dr B W Lacey, of the Westminster Hospital, London These spores are more resistant than those of *Bacillus subtilis* as obtained from the National Collection of Type Cultures and are stated by Dr Lacey to be killed only after exposure to 115°C for fifteen minutes

All glass syringes (10 ml) were used, some of them being oiled The needles were not attached On two occasions the syringes were inside metal containers, care being taken that there was an opening in the container to allow the entrance steam In the other ten instances they were in glass tub and care was taken to ensure that the plug was permeab while in the autoclave The results obtained show very clear that an efficient autoclave is all important and that it w kill these spores in the assembled syringe at a temperature 120°C at a pressure of 20 lb for twenty minutes

One theatre autoclave was successful at 15 lb for fifte minutes The others have not been tested at this pressur Two rather old laboratory autoclaves were successful 20 lb for twenty minutes, but not at 15 lb for fifteen minute One old theatre autoclave was unsuccessful on two occasion at 20 lb for twenty minutes It has since been replaced by new one It is important to note that this old autoclav successfully killed spores of *B subtilis* (as obtained from th National Collection of Type Cultures) when used on a str of filter paper

The experiments show that autoclaving at a temper ture of 120°C at a pressure of 20 lb for twenty minute as stated in the M R C leaflet on the Sterilization, Us and Care of Syringes (1945) and quoted in the letter b one of us (W N R) (Feb 19), is a satisfactory metho of sterilisation of assembled syringes

J G ALEXANDER
Hull — W N ROLLASON

Obituary

CHARLES WILLIAM BUCKLEY

M D Lond , F R.C P

Dr Buckley, whose death we announced last wee was a leading authority on rheumatism, his grea experience being gained as a spa physician at Buxton Derbyshire

Born at Derby in 1884 and educated privately, h came to London with an entrance scholarship St Mary’s Hospital and qualified in 1898 In the earl years of the century he settled in practice in Buxton but it was not until 1912 that, after many unsuccessfu attempts, he obtained appointment to the staff the Devonshire Hospital for Rheumatic Diseases, for which he was to do so much and to which he brought so much renown He became M R C P in 1923, when general practitioners were made eligible for membership of the Royal College of Physicians, and after discontinuing general practice, he was elected to the fellowship in 1933

A fine clinician, Buckley communicated his knowledge on many aspects of rheumatism His writings, always immaculately presented, appeared at intervals over the years in many medical journals and textbooks His last article appeared in 1948, his last chapter in 1955, and both were completely up to date The subject which interested him most, and to which he contributed much, was ankylosing spondylitis The first of his papers on this disease, which at that time was seldom recognised appeared in 1932 , it was based on the study of 150 cases Rather surprisingly, he produced only one book—a handbook for the general practitioner entitled *Arthritis, Fibrositis, and Gout* His greatest contribution to the specialty was his editing, first of the Royal College of Physicians reports on rheumatic diseases, and later of the *Annals of the Rheumatic Diseases*—a journal founded by the Empire Rheumatism Council and subsequently adopted by many Rheumatic Associations both in Europe and in America

He was a member of many medical societies, both national and international He served on the scientific educational, and editorial committees of the Empire Rheumatism Council, and he held office as president of the Heberden Society and of the section of Balneology of the Royal Society of Medicine He was made an honorary member of the American Rheumatism Association in 1948 Among his academic distinctions was a lectureship in chronic arthritis and rheumatism at the Postgraduate Medical School of London When he left Buxton he was made a freeman of the borough

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[1] Poulton E M , Hinden, E *Arch Dis Childh* 1953 28 392

[2] Hanson R E A S *Brit med J* 1954 i, 1038

Much as they respected him, his colleagues did not always find Buckley easy to get on with His stern appearance, and his sometimes rather pontifical manner could make him difficult to approach He was in fact a much shyer and more solitary man than was realised This was borne out recently when it was proposed to devote an issue of the *Annals of the Rheumatic Diseases* to commemoration of his 80th birthday though he reluctantly allowed his photograph to appear he forbade any further tribute to his life and works But to those of the younger doctors whom he considered anxious to learn he was kind and free from pomp, and he taught them magnificently His thoroughness and conscientiousness in the performance of his duties, his careful hospital notes written in his meticulous handwriting made a great impression on them Others of his qualities, again were appreciated especially by his associates in the town council where he was admired for his wit and skill in debate and for the breadth of vision and the underlying deep sympathy which accompanied his delightfully dry manner, and his incomparable ability to hold his own

Buckley's medical achievements are the greater when three things are taken into consideration First, during the years of his fullest activity few physicians in this country were at all interested in the rheumatic problems, and there were few rivals to keep him up to the mark. Secondly, he practised at a spa at a time when spas were unfashionable and were regarded with suspicion by members of the profession Thirdly not only did he practise in a spa but he took an active part in the affairs of its corporation (which owned the spa) being for many years a councillor and later an alderman and mayor in 1924–25 Yet he never claimed that spa treatment had any specific properties except perhaps in cases of persistent gout But he did believe and with good reason, that a spa was an excellent place in which to treat the rheumatic patient.

Apart from his medical and municipal activities he had many outside pursuits He was interested in archæology, he enjoyed his game of golf which he often played by himself or with members of his family He spent most of his holidays fishing and was for several years a member of the Flyfishers Club

Dr Buckley died at his home at Ashbourne in Derbyshire on May 28 His wife, formerly Miss Lilian Hughes, survives him with three daughters. Their only son who was a scholar at Eton died last year

HENRY ALLMAN LAVELLE

B.A., M.B Dubl

Dr H A Lavelle died at his home in Derby on May 25 at the age of 60 The son of Francis Lavelle an inspector of schools in Ireland he was one of a remarkable family of six of whom three brothers and one sister were medically qualified while another sister was a science graduate

Henry Lavelle himself entered Trinity College, Dublin as a sizar in 1914 and soon became known for originality of thought and action which he retained throughout his life After an attack of poliomyelitis in childhood he was severely handicapped by residual paralysis and although this did not prevent him from taking an active role in the defence of Trinity College during the rising in 1916 it did bar him from the Armed Forces. Instead he worked for nearly two years as an unqualified resident in general and mental hospitals both in Ireland and in England. As a result he did not qualify until 1920 when he came to the Derbyshire Royal Infirmary as a house-surgeon

In 1922 he entered general practice in Derby having married Evelyn Garnett who had been a house surgeon with him Within a year or two he had been appointed honorary obstetric physician at the Nightingale Maternity Home and honorary surgeon to the Derbyshire Hospital for Sick Children, and throughout his professional career obstetrics and the surgical diseases of children continued to be his main interests, although he never abandoned a large general practice and he was indeed a capable and much loved family doctor He was president of the Derby Medical Society in 1945 and until prevented from doing so by the illness which in 1948 struck him down and brought about his retirement from practice he hardly ever missed a meeting He frequently spoke in the discussions and could be relied on to contribute shrewd often racy and sometimes pungent comment.

Despite a very busy life he was extraordinarily well read in current literature both general and medical and he loved good conversation, which he spiced with his own subtle humour These qualities, coupled with his charm and his unconventional attitude towards many things, made him a delightful companion His interests were many and nothing gave him greater pleasure than driving his cars or tinkering with them for he was as capable with his hands in the garage as he was in the operating theatre Nor did he allow his disability to prevent him from following other outdoor pursuits, and he spent nearly all his holidays caravanning with his family usually in Cornwall where he was also able to sail and fish to his heart s content.

Henry Lavelle will be greatly missed in Derby He is survived by his widow and by two sons and two daughters One daughter is medically qualified and the wife of a Derby doctor and one son is a medical student

G F K.

ROBERT SKEOCH FREW

M.D Edin F R C.P

AT the age of 73, Dr Frew died on May 30 at Chipping Campden where he had lived since his retirement from the Hospital for Sick Children Great Ormond Street.

He was born at St. John s Newfoundland the son of William Frew and was educated at St. John s and at the Universities of Edinburgh and Berlin. Qualifying in 1905 he was house-physician at the Edinburgh Royal Infirmary and assistant to the professor of pathology His first paper published in 1909, was a contribution to the *Zeitschrift für physiologische Chemie* on the formation of lactic acid in muscle and his special interest in metabolic disorder continued when he became a pædiatrician Having worked as medical registrar at Great Ormond Street and as assistant physician at the East London Hospital for Children he was appointed in 1914 to the staff of King s College Hospital During the war he served in the Royal Army Medical Corps with the rank of major and he returned to Great Ormond Street as physician to outpatients He was also for many years physician to the Lord Mayor Treloar Cripples Hospital at Alton in Hampshire

Skilful in the handling of children Frew was also a very good teacher of undergraduates with a talent for exposition and simple classification In his investigations speculations, and innovations he was a man who thought for himself and made little attempt to reconcile his ideas with those of other people Early in his career he was a member of the Association for the Advance in Medicine by Research but as time went on he ceased to attend meetings of medical societies or to keep in touch with other people's work His *Disease in Childhood*, published in 1936 was largely the result of solitary reflection, and its emphasis on hyperphlebæmia as a cause of many of the disorders of early childhood and some of its other hypotheses, proved unacceptable

In the late war Dr Frew assumed heavy responsibility for administration at the Hospital for Sick Children and in order that he should continue to serve the hospital beyond the normal retiring age an additional appointment was created for him His son was killed in the war and he leaves a widow and a daughter

Births, Marriages, and Deaths

MARRIAGES

COHEN—WOLFSON.—On May [illegible] in London, Samuel I Cohen B.SC., M.D M.R.C.P to Vivienne L Wolfson M.B.

Notes and News

WORLD HEALTH ASSEMBLY

THE 8th World Health Assembly ended in Mexico City on May 27 On May 25 the programme and budget committee heard a statement about the Salk vaccine by Dr Frederick J Brady He said that the production of the vaccine in the United States might reach 58 million ml by the end of July, 1955 This would be sufficient to vaccinate 94% of all children from 1 to 9 years of age, which was the most susceptible period Production was expected to increase to 120 million ml by January, 1956, which would be sufficient to give two injections to approximately 60 million persons A variety of Bills were pending in Congress, including proposals to create a commission to plan and handle the distribution of vaccine, to extend the President's authority to establish rules governing control, distribution and production, and to finance the purchase of vaccine for free vaccination

The Assembly, which met under the chairmanship of Dr Ignacio Morones Prieto, health secretary of Mexico, adopted a budget of $10,203,084 for international health programmes throughout the world The Sudan was admitted as an associate member of the World Health Organisation bringing the total membership to 85

DOCTORS AND DENTAL EXTRACTIONS

THE question whether a doctor should extract teeth in an emergency was discussed at a recent meeting of the Lancashire Executive Council[1] Instances were given of children in severe pain being unable to get immediate attention A dental member said that there were not enough dentists and there would not be until the conditions of service and pay were improved Dentists had to consider other patients who had appointments, he added Mr J A Speed, clerk to the council, said that medical service was guaranteed under the Act but dental service was not He doubted whether a child's doctor could refuse to draw a tooth in an emergency In cases of difficulty, if the council's office was contacted something could usually be arranged

THE ENDOCRINOLOGY OF REPRODUCTION

THE first impression given by the May number of the *British Medical Bulletin*,[2] devoted to Hormones in Reproduction, may be one of detachment from human medicine For this there are two good reasons The first is that the physiological system is, generally speaking common to all eutherian mammals, and contributions to this fundamental scientific study have been made from all branches of biology—from zoology and animal husbandry as well as from medicine The second reason is no doubt connected with the pious and apposite reference in his introduction by the scientific editor, A. S Parkes, sc d , f r s , to his teacher, F H A Marshall, who " fifty years ago today, on 18 May, 1905," in conjunction with W A Jolly, read before the Royal Society of London a paper in which the rôles of the follicular and luteal hormones were first clearly recognised This symposium is at once a tribute and a report of progress in the subject in which Marshall was the British pioneer As Dr Parkes says " Rarely has a single subject of biological research blossomed so profusely in so short a time The fruit is now before us as an impressive body of knowledge festooned, as might be expected with loose ends of observation and deduction " This general biological approach has unexpected and stimulating aspects, as when one author illustrates hormonal effects in the ovary of the giraffe fœtus, or another remarks upon the " evolutionary oddity " of " the hypothermal scrotum—at best an inconvenient organ " The articles on chemistry and biochemistry of the hormones have on the other hand, a more orthodox approach, and may be recommended as a summing up of the present position in a subject of current therapeutic interest

In fact, every aspect of the endocrinology of mammalian reproduction seems to have been touched on , and, where they are not discussed, sources of information are indicated It is provocative of thought, to say the least, to read the only two purely clinical medical articles—Clinical Value of Hormone Estimations by Eleanor H Venning, and Hormones and Human Fertility by G I M Swyer—against the background of general biology provided by the other reviews The result may be to produce a humble frame of mind in the medical scientist, combined with some satisfaction that, despite disappointments, simple empirical approaches have yet been of some value to medicine

The British Council is to be congratulated on this production, in which all the eighteen contributors ranging from Amoroso to Zuckerman, not only originate within the British Commonwealth and work in Great Britain, but are acknowledged authorities in their respective fields

There is much talk these days of " population policy ", in this country we have a Society for the Study of Fertility and in America there is a Society for the Study of Sterility—a possibly significant difference in the direction of approach. But the study of these subjects, and any social policy which may be put forward, must be based on scientific knowledge, an all important part of which is the biological and medical basis reviewed in this number of the *British Medical Bulletin*

"ASSIGNMENT CHILDREN"

WHEN the United Nations International Children's Emergency Fund (UNICEF) heard that Mr Danny Kaye was thinking of going round the world they invited him to visit some children on the way , and the Motion Picture Industry collaborated with them in making a record of these visits, The children—of India, Korea, Thailand, Burma, and Japan—are some of those that UNICEF is helping by feeding them with America's surplus milk, healing their diseases, and teaching their mothers the elements of their craft This short film—it only lasts about 40 minutes—never puts a foot wrong Mr Kaye never lets it He himself is the least evident of the characters in the piece, he never gets a close up Most of the time all you see of him is a back, while the camera watches the sea of laughing faces confronting him, or a distant pied piper heading a running troupe of children , and all you hear of him is a sparing commentary without one touch of false emotion " A clown is a clown in any language," he says , but this clown turns himself into a ' feed," throwing the children into relief, giving them the chance to show their own story—their hunger, their confidence, their gaiety and stoicism, their undeserved disasters This is a most moving film, one which everybody should see , for, as Mr Kaye himself remarked, at the world première on June 3 " if the Motion Picture Industry or anyone else can help us to understand what is happening to children we may be further on the way towards understanding ourselves "

CENTENARY OF A SANATORIUM

IN the early 1850s the committee of the Brompton Hospital began to consider constructing a sanatorium On Oct 1, 1855, as the result of the committee's initiative the National Sanatorium for Consumption and Diseases of the Chest was opened at Bournemouth with accommodation at first for fifteen male and fifteen female patients This month the Royal National Sanatorium, as it has since become, has been celebrating its centenary In its hundred years of activity the death rate from pulmonary tuberculosis has fallen from nearly 28 to less than 2 per 10,000 population

YOUNG EATERS

Mr F Le Gros Clark has that invaluable possession, a perennially fresh mind He has been writing about nutrition for many years, and it might be supposed that he had exhausted every approach to even this many sided topic Not a bit of it in a new little book[1] written for the National Society of Children's Nurseries he has asked and answered the questions likely to occur to a mother with her first baby and very sensible questions they are, and most refreshingly answered Instead of plunging her into a morass of unfamiliar terms and weighing her down with the latest news of vitamins, he begins with a short outline of the physiology (though that word is never mentioned) of feeding and growth, drawing her attention to three components of her baby—his muscles and organs, his bones and his fat This naturally leads to a longer account of each of the three, and of the foods which help to make them Protein naturally gets a good deal of space, and Mr Le Gros Clark explains how a mixed diet can supply the various amino acids (a word used only once, at the end of the explanation) needed by the body, which then selects and rearranges them to suit itself This he does by

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[1] *Manchester Guardian* May 26 1955

[2] *British Medical Bulletin* vol 11, no 2 Published by the Medical Department the British Council Pp 96 15*s*

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[1] A B C of Food and Child Feeding London National Society of Children s Nurseries, 45 Russell Square W C 1 Pp 49 1*s* 9*d*

drawing the analogy of a bead bag from which beads may be taken to build up another bag of a different pattern. He writes of the calcium-containing foods which build the bones the energy stores of the body in the liver and muscles (the word "glycogen" is not mentioned) and in the fat deposits the nature of common foods emphasising that most of them contain more than one of the three main components and finally the four main vitamins—not as "food" but as "traffic controls" organising the materials from our food into the structure of our bodies. In the same lucid and simple way he discusses weaning and table manners unobtrusively reminding the mother in every sentence that she will be dealing not with a "model baby" but with an individual of strong personal views.

The book is described as a short introduction for the use of student nurses but well though he has served the nurses it is the ear of the mother which Mr Le Gros Clark has hoped and deserves, to catch.

GENETIC CHANGES DUE TO RADIATION

SPEAKING lately at the University of Chicago Dr Willard Libby a member of the U.S. Atomic Energy Commission, read the following statement prepared by members of the commission's advisory committee for biology and medicine[1]:

> "The radiation produced by fall-out from atomic weapons ts as well as from present and future peaceful applications of clear energy will result in additional mutations in human genes. The number of these cannot be estimated accurately at this time. the current rate of irradiation from fall-out among the four llion children born each year in the United States perhaps from a ndred to several thousand may carry as a result of this irradiation mutated gene.
>
> "At most a small percentage of these genes will produce any noticeable effects in the first generation. Only slowly over hundreds years will the majority of these radiation induced genes become parent, in a few individuals at a time usually by causing a less n normal development or functioning of the person concerned will be impossible to identify these individuals among the large mber of similar ones affected by genes already present in the pulation due to accumulated spontaneous mutations.
>
> "No measurable increase in defective individuals will be observ at any time as the result of current weapons tests since the w radiation-induced defectives will not change measurably the mber of about forty thousand defectives who will occur spon eously among the four million births of each year in the United tes. It may be pointed out that no significant change in the rcentage of malformed children has been observed among those nceived after the war whose parents had been exposed to the mic bombs in Hiroshima and Nagasaki.
>
> "The foregoing conclusions apply only to the genetic effects weapons tests carried out at the present level and the foreseeable ce-time uses of atomic energy. The genetic effects of a generalised ar war would be one of many catastrophic consequences of such saster."

MANAGEMENT OF LABOUR

A NEW film made by Dr Grantly Dick Read and entitled *Childbirth without Fear* is not so much a means of instruction as of propaganda. But it is none the less impressive for that. The deliveries of four unselected mothers are shown quite kly and the expressions on these women's faces are memorable. e is an introduction to each case by Dr Read and brief pses of the earlier stages of labour—sufficient however ggest the general scheme of management. There is little iption of the antenatal preparation of the mothers—a wise sion in a short film with little time to spare especially antenatal preparation has been over publicised at expense of the more important subject of management ng labour.

he question arises, as it always does with such films for m is it intended? This one could usefully be shown to ical groups as a prelude to discussion. It could also ently well be shown to expectant mothers and their bands provided the showing was well supervised and oduced for there is nothing in it that is not encouraging. the other hand some teachers might hesitate to show it to ents because there are points in technique that are open isagreement.

ainless *Childbirth* is a film on the work of Dr Fernand naze made for showing to mothers as part of Dr Lamaze's gramme of antenatal preparation. It would not be suitable that purpose in this country since it shows a distressed mipara in the second stage. The most impressive point de in the film is that the labouring mother must never be t alone—trained or untrained—for it is in loneliness that the rors and incoordinations of behaviour in childbirth appear. Lamaze does not use only doctors and midwives the n shows an aide or orderly, trained in the method helping the mother to concentrate on her breathing rather than on her discomfort.

This film is suitable for midwives, students and physiotherapists. The teacher showing it needs to make it clear that the techniques of delivery are not an intrinsic part of the method but are those commonly practised in France. Apparently in the Soviet Union where Dr Lamaze learnt his technique ideas about the management of delivery are similar to those in this country.

PHILADELPHIA CHILDREN'S HOSPITAL

THE Children's Hospital in Philadelphia was established in 1855 and during the centenary celebrations last week[1] a block and gavel made from the wood of a plane tree which grew in the garden of the Hospital for Sick Children Great Ormond Street were presented to the hospital by Dr Alan Moncrieff Nuffield professor of child health in the University of London, who was a special delegate and spokesman at the proceedings for Great Ormond Street and other British children's hospitals. He recalled that the two institutions in London and Philadelphia were the first children's hospitals in the English speaking world (Great Ormond Street was just three years older).

Royal College of Physicians of London

Dr K. M. A. Perry is to deliver the Ernestine Henry lecture at the college Pall Mall East S.W.1 on Tuesday June 21 at 5 P.M. Dr Perry will speak on Pulmonary Diseases Associated with *Metallic Oxides*.

Dr Ian McLean Baird working in the department of therapeutics at the Royal Infirmary Sheffield has been appointed Leverhulme research scholar of the college for 1955.

Royal College of Surgeons of England

Faculty of Anæsthetists.—At a meeting of the board of the faculty on June 1 Dr Frankis T Evans was elected dean and Dr R F Woolmer was re-elected vice-dean for the ensuing year.

Royal College of Surgeons in Ireland

At a meeting of the college on June 6 the following were elected:

President Ian Fraser, vice-president A B Clery *other* members of council J F L Keegan, R. A Stoney J F L. Devane A A McConnell, T O Graham William Doolin Frederick Gill T G Wilson M P Burke R R Woods S F Heatley J H Coolican T A Bouchier Hayes, N A Kinnear D J Riordan F W L. Thompson F A J M. Duff D W Montgomery J M M Curtin.

Osler Club of London

To mark the centenary of the birth of Stephen Paget the club is to meet jointly with University College Medical Society at University College Gower Street W.C.1 on Thursday June 16 at 8 P.M. when Prof G P Crowden will speak on Pioneers in Experimental Physiology and Dr J H Baron on The Brown Dog of University College.

Royal Sanitary Institute

The following are among the forthcoming sessional meetings:

London.—Mr P G Shute: Rôle of Mosquitoes in the Spread of Myxomatosis and Suggestions for their Control; at 2.30 P.M. on Wednesday June 22 at the institute 90 Buckingham Palace Road S.W.1.

Oldham.—Dr J T Chalmers Keddie: Care of the Mentally Ill and Mr H V Cas: Housing Repairs and Rents Act 1954; at 10 A.M. on Friday July 8 in the assembly room, Town Hall.

London.—Dr J D Kershaw: Public health Nurse of the Future; at 6 P.M. on Wednesday, July 13 at the institute.

Taunton.—Dr Hugh Morrison: Changing Face of the Control of Infectious Disease and Sir Arnold Waters: Taunton Sewage Scheme; at 10.30 A.M. on Thursday July 21 in the council chamber Shire Hall.

Medical Society for the Care of the Elderly

At the annual meeting of this society on May 7 the following were elected to the executive committee:

President, Lord Amulree; hon vice-presidents Dr J H Sheldon and Dr E L Sturdee; hon treasurer Dr W Morton; *hon secretary* Dr A. N Exton Smith; hon deputy secretary Dr P Arnold, other members Dr J Agate Dr O T Brown Dr K J G Milne Dr L Nagley, Dr O Olbrich *Prof* R. E. Tunbridge Dr M. Warren, and Dr T S Wilson.

Hypnotherapy Group

At a *meeting* at 1 Wimpole Street London W 1 on Wednesday June 15 at 8 P.M. Dr H J Shorvon will discuss the Use of Drugs in the Induction of the Hypnotic State.

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[1] *Manchester Guardian* June 6 1955

[1] *Times* June 3 1955

Royal Appointment

Air Commodore Denis Aymard Wilson has been appointed an honorary surgeon to the Queen in succession to Air Vice Marshal E D D Dickson, who has retired from the Royal Air Force

Collegium Internationale Allergologicum

The second symposium of the Collegium, dealing mainly with Migraine and Vascular Allergy, is to be held in Basle on July 3–8 The president is Dr D Harley, 19, Queen Anne Street, London, W 1 , and the secretary is Dr P Kallós, Sundstorget 3, Helsingborg, Sweden

Commonwealth Bursaries

Awards under the Royal Society and Nuffield Foundation Commonwealth bursaries scheme include the following

Dr A A. Kinnear *Institute for Pathology, University of Pretoria*, to study endocrinological techniques at Birmingham from July to September, 1955

Dr. J H D Millar neurologist Royal Victoria Hospital, Belfast, to study electrocorticography at the Montreal Neurological Institute from September to November 1955

Panel on the Composition and Nutritive Value of Flour

The panel set up by the Government, under the chairmanship of Lord Adrian, P.R S , to investigate the composition and nutritive value of flour (see *Lancet*, May 14, 1955, p 1021) has held its first meeting Persons or organisations wishing to submit evidence are invited to send this in writing to the secretary, Miss B M Shedden, 10, Whitehall Place, London, S W 1, by July 9

Appointments

BALCH, H W., M B Aberd , D PHYS MED S H.M.O , hospitals and clinics in Aberdeen, North Eastern R.H B

BENTON F M., M B Manc F F R , D M.R.T consultant radiotherapist, Hogarth Radiotherapeutic Centre at Nottingham General Hospital, and associated clinics in the area Sheffield R H B

BRAIMBRIDGE, M V , M.B Camb , F R C.S surgical registrar, East Suffolk and Ipswich Hospital, Ipswich

CAPPER LEONARD, M B Lond., M R.C P asst chest physician, Cambridge area Chest Clinic, East Anglian R.H B

DUFFY, JOHN M.D N U I , F R.C.P I , D P H T D D medical superintendent, James Connolly Memorial Chest Hospital, Blanchardstown, co Dublin

FRASER, W D M B Glasg , F.F R., D.M R T radiotherapist in charge, Hogarth Radiotherapeutic Centre, Nottingham General Hospital and associated clinics in the area Sheffield R H B

HAIGH R D , M B Leeds D P H , D OBST senior asst county M O and school M O , Brighouse Corporation, Elland urban district council, and West Riding county council

HAMILTON, E M , M B E , M B Belf D.P H M.O and asst. county M O borough of Wallingford urban district of Wantage, rural districts of Wallingford and Wantage

NELSON, M. P M R C.S D P M. medical superintendent, Sandhill Park hospital group, Bishops Lydeard, near Taunton

PARRY, W H M B Lpool, D P H. senior asst M O , city of Liverpool

SHARPLES, N A , M B Durh , D.M R.T asst radiotherapist St Thomas's Hospital S E 1

VINCENT, H R M.R.C S deputy group medical superintendent, county and city of Perth General Hospitals, and Bridge of Earn Hospital

Newcastle Regional Hospital Board:

HAWKINGS, J R , M B Brist D P M consultant psychiatrist Winterton Hospital, Sedgefield, co Durham

IRWIN, DAVID, M B Glasg , D P M. consultant psychiatrist and deputy medical superintendent, St George s Hospital Morpeth Northumberland

LASCELLES, C F , M B Aberd D.P M asst psychiatrist (S H M O) Cherry Knowle Hospital, Ryhope near Sunderland co Durham

PILISZEK S T M D Warsaw asst psychiatrist (S H M O), Winterton Hospital Sedgefield co Durham.

Hospital for Sick Children, Great Ormond Street, W C 1

FAIRBURN A C , M B Lond house-physician

FRANCIS M J , M B Brist , D C H D.A junior resident anæsthetist

LOURENSZ, D A L M B Ceylon resident registrar to the ear nose and throat department

MCKENDRICK THOMAS M B Lond D C H house physician

MASTERTON, J P , M B Glasg D OBST house-surgeon

MYERS N A A M B Melb F R A C S house-surgeon

RICHARDSON F L , M B Birm M R C P asst medical registrar

Appointed Factory Doctors

FORSTER D M M B Birm Brownhills Stafford

MILLAR G R. M B Edin Dalkeith Midlothian

International Vitamin-E Congress

The Third International Vitamin E Congress is to be held in Venice on Sept 5–8 The secretary's office is at Via Pietro Verri 4, Milan, Italy

Congress of Gastroenterology

The fifth International Congress of Gastroenterology will be held in London from July 18 to 21, 1956, under the presidency of Dr Thomas Hunt The main subjects for discussion will be ulcerative colitis, premalignant conditions of the gastro intestinal tract, and non malignant diseases of the œsophagus

International Conference of Medical Librarians

An International Conference of Medical Librarians and Reference Librarians will be held in Brussels on Sept 10. This conference is being organised in connection with the International Congress of Libraries and Document Centres, which will take place from Sept 11 to 18 Further information may be obtained from Miss Ch de Looze, Librarian c/o Œuvre Nationale Belge de Défense contre la Tuberculose, 56, rue de la Concorde, Brussels

Diary of the Week

JUNE 12 TO 18

Tuesday, 14th

ROYAL SOCIETY OF MEDICINE, 1, Wimpole Street, W 1
8 P.M *Psychiatry* Prof Torsten Sjögren (Stockholm) Alzheimer's and Pick's Disease
INSTITUTE OF OBSTETRICS AND GYNÆCOLOGY
NOON (Queen Charlotte s Hospital Goldhawk Road, W 6 Dr W G Oakley Diabetes and Pregnancy
INSTITUTE OF DERMATOLOGY, St John s Hospital, Lisle Street, W C.
5 30 P.M Dr J O Oliver Serology and Laboratory Diagnosi of Syphilis
SANDERSON WELLS LECTURE
4 30 P M (Middlesex Hospital, London, W 1) Prof. R. A McCance, F R S Old Thoughts and New Work on Bread White and Brown

Wednesday, 15th

INSTITUTE OF OBSTETRICS AND GYNÆCOLOGY
4 30 P.M (Chelsea Hospital for Women, Dovehouse Street S W 3) Mr Aubrey Goodwin Wertheim's Hysterectomy
INSTITUTE OF DISEASES OF THE CHEST, Brompton Hospital, S W
5 P.M Dr George Simon Pitfalls in Chest Radiology
INSTITUTE OF DERMATOLOGY
5 30 P.M Dr Henry Haber Cutaneous Manifestations o Syphilis
CIBA FOUNDATION
5 P.M (26, Portland Place, W 1) Prof H Olivecrona (Stockholm) Hypophysectomy in Diabetes

Thursday, 16th

POSTGRADUATE MEDICAL SCHOOL OF LONDON, Ducane Road, W 1
4 P.M. Dr Ian Gilliland Exophthalmos
ROYAL SOCIETY OF MEDICINE
10 A.M (Anatomy Theatre, Downing Street, Cambridge *Laryngology and Otology* Mr Donald Broadbent Psychology of Hearing Mr Alan Bowen Davies Chron Ear Disease in relation to Insurance and Employment
INSTITUTE OF CARDIOLOGY
11 A.M (National Heart Hospital, Westmoreland Street W 1 Dr Lewis Dexter (Boston) Selection of Cases for Cardi Surgery
INSTITUTE OF DISEASES OF THE CHEST
5 30 P M Dr P V Benjamin Programmes for Tuberculos Control in India
INSTITUTE OF DERMATOLOGY
5 30 P M Dr Haber Basal-cell Epithelioma
ROYAL SOCIETY Burlington House, W 1
4 30 P M Prof C H Best, F R.S (Toronto) Dietary Factors in the Protection of the Liver, Kidneys Heart, and other Organs in Experimental Animals the Lipotropic Agents

Friday, 17th

POSTGRADUATE MEDICAL SCHOOL OF LONDON
2 P M Dr A C Thackray Mucous-gland Tumours
ROYAL SOCIETY OF MEDICINE
10 A M (Anatomy Theatre Downing Street, Cambridge *Laryngology and Otology* Mr A S H Walford Dr A Crampton Smith Dr J M K Spalding Modern Indications for Tracheotomy
INSTITUTE OF CARDIOLOGY
5 P.M (1, Wimpole Street W 1) Dr Dexter Atrial Septal Defect (St Cyres lecture)
INSTITUTE OF LARYNGOLOGY AND OTOLOGY, 330 Gray s Inn Road W C 1
3 30 P M Mr W D Doey Sinusitis and Chest Disease

Saturday, 18th

BIOCHEMICAL SOCIETY
11 A M (Biochemistry Department University of Oxford Scientific papers

MENTAL HEALTH
DESPITE
MENTAL RETARDATION *

A. F ALFORD
C.B.E., M B Brist
SENIOR MEDICAL OFFICER, MINISTRY OF EDUCATION

MENTAL deficiency is not an illness or a disorder of mind, but rather an arrested or incomplete development of brain, usually from birth leading to a diminution of intellectual powers relative to the chronological age † Unfortunately children who are born with this deficiency of mental powers receive less sympathy and understanding than children who are physically handicapped Those who suffer from a disability which can be *seen* usually receive warm hearted pity, even though the nature of the handicap may not be fully appreciated or understood But those who suffer from a mental retardation rather tend to raise in the public mind a sense of repulsion and even an emotional dislike This attitude is due, primarily to a lack of knowledge about these children as regards both the genesis of their retardation and its effect on their intellectual and emotional well being the possibilities of the child developing such powers as he has and becoming a useful citizen are ignored

This present attitude of so many is greatly to be deplored For if mental defectives are not received naturally and without bias in the community but are shunned or treated as outcasts, their mental health suffers leading frequently to introspective emotional disturbance or to aggressive antisocial behaviour

The Parents Feelings

Parents attitude towards their defective offspring may leave even more to be desired The parent-child relationship should be the same as in normal families, and yet often, particularly where the parents are intelligent is clouded by a deep sense of guilt because they imagine that the handicap is their fault, or that they being punished for past misdeeds

This sense of guilt is chiefly based on lack of knowledge the possible causes of mental deficiency Thirty or ty years ago mental deficiency was thought to be caused entirely by heredity if a child was mentally defective it was taken as a sign that his parents—or their parents before them—were defective too Since those days, however it has become abundantly clear that, though heredity remains a prime factor there are other causes which produce subnormality In families unimpeachable heritage mentally defective children found. Indeed in most gatherings of professional and intelligent people there is likely to be at least one family containing a mentally subnormal child. Proof of causation still evades us Certain postnatal illnesses such as meningitis and accidents are readily accepted causes But many theories have been advanced which implicate among other things endocrine deviations or biochemical reactions in utero the rhesus factor and natal asphyxia and cerebral damage during birth Although none of these theories would explain more than a small fraction of these indeterminable cases, it does bring consolation to parents and removes their sense of guilt to know that their child may be as he is through causes other than heredity

But, even if this sense of guilt is lessened or removed parents find it difficult to accept a defective child in the family The less intelligent parents frequently may not acknowledge the presence of the disability at all It is not easy, even for intelligent parents to understand that a child can have a world which is different in any way from their own, that his perspective and outlook cannot be the same as theirs, and that the future does not hold a cure for an innate mental disability They do not realise that the lower the intelligence the greater the shrinkage of the child s world until, in the lowest grades the world is the child s immediate environment, the part of a room or garden in which he happens to be at that moment. They are unwilling—subconsciously, if not consciously—to accept that a defect of mind remains throughout life Thus, false hopes are aroused which, when they are dashed, lead to resentment and even despair

Such feelings and the sense of guilt as well can create a vicious circle An unnatural barrier is set up between parent and child which not only prevents a mother experiencing the full joy of motherhood but may also prevent her showing any of the love she feels for her child This can have a disastrous effect on the emotional development and well being of the child whose reaction in turn may loosen the bonds of mother love to such an extent as to bring about partial or even complete rejection of the child

The point to be driven home to the public at large, as well as parents is that every child who is handicapped either in mind or body should be looked upon not as a defective but as a normal child, with a deviation from normality in one particular respect This positive approach tends to focus attention on potentialities instead of imperfections

When a child is born who is obviously mentally defective what should be said to the parents? The parents are keyed up physiologically and emotionally, and such a child is a bitter anticlimax to their hopes and expectations It is not right to leave them in a state of ignorance for long for the sooner they realise their misfortune the better they will be able to cope with the problem If such knowledge is withheld too long the mental health of the parents and subsequently of the child will often suffer more damage the late repair of which becomes increasingly more difficult—as experience has proved over and over again But the information must be given judiciously, tenderly and with much sympathetic understanding and patience There is more than one way of saying the same things care must be taken to use the way which will help the individual most to accept what has happened and to make the best of it

Later on if the parents have a sense of guilt or despair and a vicious circle is set up it may be broken by the family doctor or any other person who is able to approach the problem with wisdom understanding and sympathy He can help the parents to face reality by explaining what they feel as simply as possible by being willing to listen and by answering their questions, however indefinite and vague Once the agitation of the parents' minds has been calmed by the acceptance of the situation, their mental health improves and that at once has a favourable effect on their child

Education and Self-respect

The variability of intellectual deficiency is infinite But whatever the intellectual level the aim must always be to nurture and develop to the fullest extent in early life the intelligence there is so as to enable a child to live a life to the limit of his powers and to equip him to

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World Federation for Mental Health A paper read last August at Toronto before the Fifth International Congress on Mental Health under the title Some of the Mental Health Aspects of Mental Deficiency

Mental deficiency is not defined in the same way in all countries In England and Wales, since the Education Act of 1944 the term has referred only to those children who by reason of a mental disability cannot be educated in schools. Those who can be educated in schools but need some special help are classified as *educationally subnormal* and that is the group with which this paper is chiefly concerned take his place, however lowly, in the world around him, and to make him acceptable to his fellow men

If an attempt is made to drive a child too far, he will feel frustrated by his failure and may well sink below the level he could otherwise comfortably reach If a child is not stretched adequately, then he will stagnate and lose his self-esteem and respect A child who lives fully up to his intellectual capacity has also gone a considerable way toward the contentment and happiness which are the foundation of mental health

Furthermore, the retarded child must have within him a sense of self-respect, if his mental health is to flourish Many components, acting in unison, help to instil this self-respect Uninhibited mother-love and good family relationships, full development of intellectual powers leading to achievements both in thought and action, fostering of independence, belief in and realisation of innate abilities, and, above all, acceptance by others—all exert a tremendous influence on the growth of self respect Obscured by mental deficiency, this may appear of little consequence to others, but to the child it is vital and extremely satisfying It is not brought about by development suddenly or by concrete effort on the part of others It waxes imperceptibly as the early years pass, chiefly through the external influences and guidance of others, until self-respect prevails Then lies ahead a life full of promise

A child can be helped to develop his mental powers to their fullest extent if he is given the right education and training For this it is essential to have a sound knowledge of the diverse combinations of attributes and of the variations of mental processes in the intellectual make up of mentally retarded children This knowledge can only be acquired by experience, based initially on a profound understanding of normal children and of the very wide limits of normality For, until this has been done, the significance of deviations from normality can neither be fully appreciated nor assessed Because each child is an individual, there are no easy rules which govern the understanding of these retarded children Every one must be considered as a separate entity, and his needs met in such a way as to encourage the promotion of his good mental health

Although a mentally retarded child will in intelligence be well below the average for normal children of the same age, he will have some mental qualities which range themselves above or below his general level What counts is that he has some qualities above *his* average, the general average does not matter Further, it is essential to remember that these children do not all possess the same characteristics Not only do they differ in intelligence, but at each level they also differ in temperament, emotional stability, and, above all, in upbringing and home background The results of these differences show themselves in uneven development They do not have poor memories for everything, they remember well only that which they comprehend or which has taken their fancy They may be able to repeat with ease simple poems or hymns, but be unable to recall anything of a lesson which was over their heads They can often concentrate well on something which interests them and yet be scatterbrained where academic subjects are concerned Sometimes, where written work is not required, they may approach closely to the interests and abilities of normal children in, say, handicraft or observation of Nature, in singing or physical movement There is scarcely one who has not some relatively strong point capable of being utilised by a watchful teacher as a basis for wider and more fruitful progress It is seldom that there is complete apathy, denying one a starting-point on which to build, but the building is a highly individual process which cannot take place in large groups If they are to advance, individual methods are

A sense of achievement is of immense importance to these children Every one of us derives great satisfaction from the accomplishment of a task, and the more difficult it has been the greater will be the satisfaction In mentally defective children the satisfaction secured through any achievement is always profound and it may be out of all proportion to the nature of the task It brings with it, as a natural sequence, a sense of mental well being, the corollary of good mental health On the other hand, while nothing succeeds like success, nothing is so devastating to the mental health of a defective child as to offer him lessons which are beyond his powers of comprehension If these are given, frustration, irritability, impatience, and many other manifestations of unsatisfied achievement will show themselves, and thes may be the seeds of emotional disturbances or of anti social behaviour later, which every effort should b made to prevent Hence, in the field of education teacher should concentrate from the start on the abilities an aptitudes which are above the child's average an should give lessons and tasks which are within the child' compass This, of course, means that the education mu be related more to the level of intelligence than t chronological age

Social Adjustment

Once action has been taken to secure appropriat education for a mentally subnormal child, results, as rule, are quickly apparent They are obtained mo rapidly where the change in environment is greate —for example, when a child is transferred from a ordinary school with large classes, where the teacher h little time for him, to a special school which caters f children of his intellectual level in smaller groups Th first change is usually in behaviour, for most teache realise that without social training there is likely to little progress in the more formal aspects of educatio They therefore concentrate at first on making the chi feel secure, on demonstrating that adults are rea interested in him, and on making it clear that they not judge him only by his success or failure in sch work Children with appalling histories of destructivene delinquency, tempers, aggressiveness, or truancy ha settled down quickly under a new régime and after t first few weeks have given no trouble at all After t improvement in conduct comes a blossoming of t personality, often accompanied by improvement carriage and physique, increased weight, and bett complexion The children become more agreeable to li and work with, they settle down with increased se confidence and self-respect to tackle their school wo and to use their intelligence, meagre though it may b to the best advantage The girls can be taught t appreciate and to develop habits of cleanliness and ord in the home, whilst the best learn to do some of t duties which fall to the lot of the housewife Bo usually have some instruction in practical work wh sometimes leads on to a skilled craft, but which, in a case, contributes towards the development of gener handiness The great justification for this régime i however, its success in making these children more social acceptable and adaptable

The social training of these children is of immens importance and of far more significance to them th mere educational attainments The extent to whi they are accepted as agreeable individuals by and in community is directly proportionate to the degree o their social adjustment A boy who is cheerful, willing and obedient, and yet perhaps unable to read or write will be accepted, whereas another who can do both relatively well, will be shunned or disliked on account of his lack of social qualities This attitude of the community has a direct reaction on the mental health of each boy The former boy feels that he has fulfilled his main ambition of being somebody in the eyes of others, thus giving him a sense of citizenship, and above all, of usefulness The latter boy has a feeling of failure and frustration or grievance and ill will against society, all of which breed discontent and unhappiness leading to emotional difficulties and maladjustment and perhaps even to delinquency and crime

In order to inculcate a sense of good mental health in mentally defective children several fundamental conditions must be fulfilled The most vital one is that the child must be brought to accept good social standards principles, and customs through education and training within a suitable environment Environments shape the individual; everyone can be affected by his environment be good or ill An unsatisfactory atmosphere produces an unsatisfactory person

The part that associates and companions play is also of much significance As the mental powers of a child are reduced so are diminished his powers of appreciation of right or wrong or of deciding things for himself He is easily led, he is swayed readily by others and he is apt to do things without realising their import He becomes very responsive to the influences, for good or evil, of those around him If his associates have low moral principles or delinquent propensities their influence on him is corrupting and he may easily succumb to their wiles and depravities His own mental health will suffer sooner or later as a result of discredit and disgrace leading to a declining self-esteem On the other hand if his companions are honest and of good character he will respond just as readily Through spending his time in a good atmosphere his mental health will profit Every effort therefore, should be made to ensure that so far as is possible these children are shielded from unsavoury associates.

Employment and Contentment

After education or training has ended employment has a direct bearing on the mental well being of these children They have an urge to be like others to be able to do things and above all, to have a job which earns them money Suitable employment is not always easy to obtain but when it is found to fit a young person his satisfaction is very real and he feels that he has proved his worth his independence and his usefulness Lack of intelligence is not by any means a bar to gainful employment In many of the unskilled and semi skilled occupations of modern life what counts in obtaining and retaining a job is not so much specific skill, literacy or information as steadiness reliability honesty and the ability to get on well with workmates and the foreman—in fact qualities of character and social development which can be acquired even by those of poor intelligence if they are well taught and are not discouraged by being forced to attempt what is beyond them. Because of their mental deficiency discontent or dissatisfaction about the relative lowliness of a job or the poorness of the pay does not arise He does not mind incessant repetition of the same action or activity it is something which has to be done by someone and *he* can do it. But if he is to enjoy his work to the full others around him must be aware of his limitations and must be willing to be tolerant kind and understanding

To sum up the ultimate aim with these children should be to make them happy and contented. The starting point is to regard them as normal children with an intellectual deviation They can be helped by social training and education to live a full life within their limitations giving them a sense of satisfaction worth and usefulness. With happiness will come mental health and a child who has good mental health even if he is mentally defective is an asset to the community and therefore to the country It is a challenge to everyone to help all mentally defective children to achieve the mental health which is the birthright of every human being

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GLUTAMIC ACID IN HEPATIC COMA

J M. WALSHE
M.A M.B Camb M.R.C.P
From the Medical Unit University College Hospital London

RECENT research into the biochemistry of hepatic coma has directed attention particularly to disturbances of nitrogen metabolism

Previously I have pointed out (Walshe 1951) how disturbed metabolism of amino acids might inhibit the metabolism of glutamic acid in the brain, leading to accumulation of intracellular ammonia

Other workers have studied blood ammonia levels in hepatic coma (Schwartz et al 1953 Traeger et al 1954 McDermott and Adams 1954 Bessman et al 1954 Singh et al. 1954 Riddell and McDermott 1954, Sherlock et al 1954) Analysis of the published results shows great discrepancies in the values given for normal blood 'ammonia levels in the different groups and though the blood ammonia" level is usually raised in patients in hepatic coma or pre-coma, there is no more than a fair correlation between this and the state of consciousness It has been established however that ammonium salts and ammonium ion-exchange resins when given to *patients with advanced hepatic cirrhosis, may produce a* syndrome closely mimicking hepatic coma (Van Caulaert et al 1933, Fuld 1933 Gabuzda et al. 1952), and intravenous ammonium chloride will produce convulsions in rabbits—an action prevented by glutamic acid (Sapirstein 1943)

In a preliminary communication I described the results obtained with large doses of glutamic acid given either intravenously or by mouth to patients in hepatic coma resulting from chronic liver diseases (Walshe 1953) Five episodes of coma in 3 patients were treated with glutamic acid, and the results were sufficiently encouraging to merit further study

Subsequent reports on the use of glutamic acid in hepatic coma have been conflicting Some workers confirm the beneficial action in patients with chronic liver disease (Priest et al 1953 Whitehead et al 1954 Riddell and McDermott 1954 Walley 1954 H Blalock jun personal communication) whereas others have not been convinced of any benefit (Singh et al 1954 Davidson 1954, Sherlock et al 1954) There appears to be general agreement that, in the coma of acute hepatic necrosis, glutamic acid does not alter the course of the illness (Calvert et al 1954 Whitehead et al 1954 Riddell and McDermott 1954)

Since my preliminary communication in 1953 a further episode of coma in 1 of the original cases and episodes of coma in 4 further cases of hepatic cirrhosis and in 2 cases of massive hepatic necrosis have been treated with glutamic acid in this hospital Glutamic acid appears to influence favourably the coma of hepatic cirrhosis but not that of massive hepatic cirrhosis.

Case reports

HEPATIC CIRRHOSIS

Case 1—A man aged 60 who admitted to considerable spirit-drinking over many years, complained of losing weight for six months and increasing jaundice for one month There were no associated constitutional disturbances.

On examination he was deeply jaundiced, his spleen was impalpable and his liver dullness was much reduced to percussion; but fœtor hepaticus was present The protein-flocculation tests were strongly positive and the serum albumin level had fallen to 3·0 g per 100 ml The prothrombin concentration was too low to allow needle biopsy of the liver to be done with safety

Treatment and course—With rest in bed and adequate diet the patient's condition improved considerably and he left hospital almost anicteric after a stay of ten weeks. Three months later he was deeply jaundiced and mentally confused ascites was present he was extremely drowsy and his tendon jerks were very brisk, but he had no ankle clonus and the plantar responses were flexor. Oral glutamic acid 20 g. daily was started, and this coincided with a rapid improvement in his mental condition. After three days glutamic acid was withdrawn, and within twelve hours he became confused and incontinent of urine. Glutamic acid was restarted by mouth, and in the next forty-eight hours he returned to normal consciousness. Withdrawal of glutamic acid was again followed by coma within twenty four hours, with increased muscle tonus in the legs and bilateral extensor plantar responses. A slow intravenous infusion of sodium glutamate was started, 17 g. being given over eight hours. At the end of this time the patient was conscious and could answer simple questions, and the plantar responses had reverted to flexor. Maintenance doses of oral glutamic acid were given, but despite this he returned through confusion to coma during the next five days. After three days' coma he was given intravenous sodium glutamate 46 g. in twenty four hours; at the end of this time he could answer simple questions but was drowsy and resented interference. No glutamic acid was given after this, and the patient lapsed into coma and died three days later.

Necropsy revealed advanced diffuse fibrosis of the liver, which weighed only 840 g.

Case 2.—A man, aged 56, had been in good health until a year before admission, when he began to feel vaguely unwell and lost his appetite. After eight months he had a large hæmatemesis, which necessitated admission to his local hospital, where he was transfused and hepatic cirrhosis was diagnosed. After his return to work he became jaundiced and noted swelling of his legs and abdomen. There was a history of considerable drinking of beer and spirits during the war years.

On admission to University College Hospital he was mildly icteric and had multiple vascular spider nævi, ascites, œdema of the ankles, and fœtor hepaticus. There were no abnormal signs in the central nervous system (C.N.S.).

Treatment and course.—A fortnight after admission he had a very large hæmatemesis and, despite a transfusion of 6 pints of blood, passed into deep coma, with knee and ankle clonus and bilateral extensor plantar responses. There was then gross amino aciduria. After twenty-four hours in deep coma his condition was deteriorating and he was therefore given sodium glutamate 35 g. intravenously in twenty four hours. Consciousness was returning by the end of this time and was normal after a further twenty four hours. A month later he had another very large hæmatemesis and died before treatment could be started.

Necropsy showed that his liver was deeply scarred by dense bands of fibrous tissue and weighed 1200 g.

Case 3.—A man, aged 38, had been in good health until four years previously, when his abdomen and legs began to swell. He was admitted to hospital, and hepatic cirrhosis was diagnosed. His symptoms cleared completely after treatment by rest in bed and a high protein diet. He remained well for four years until December, 1953, when he was admitted to University College Hospital after having a hæmatemesis. He was found to have hepatic fibrosis and portal hypertension. While in hospital he had two further hæmatemeses on consecutive days and, despite adequate blood replacement, became comatose. He had a strong fœtor hepaticus.

Treatment and course.—After a day in coma he was given sodium glutamate 23 g. in eight hours, and four hours later he had regained consciousness and was mentally alert and rational. The following week he was sufficiently well to have an operation for splenectomy and lienorenal shunt. He remained in good health for six months, at the end of which he had yet another hæmatemesis followed by the development of a precomatose state and a raised blood-" ammonia " level (175 µg. per 100 ml.). His condition improved with glutamate therapy, and the blood " ammonia " level returned almost to normal (75 µg. per 100 ml.). Later there was an episode of severe rectal bleeding, from which he died.

Necropsy revealed thrombosis of his lienorenal shunt and his superior mesenteric vein, and infarction of much of his small bowel.

Case 4.—A woman, aged 39, had had an illness with abdominal pain and jaundice six years before she was first seen in University College Hospital. Two years after her first symptoms she developed ascites and œdema. The diagnosis of cirrhosis of the liver was confirmed by needle biopsy. At first the retention of fluids was controlled by ion exchange resins and a low salt diet, but later paracentesis abdominis had to be resorted to with increasing frequency. In August, 1954, forty eight hours after a routine tapping she became drowsy, complained of severe anorexia and headache, and developed a severe irregular tremor of her hands, with ankle clonus and bilateral extensor plantar responses. Fœtor hepaticus was not detected. Hepatic coma appearing imminent, she was given sodium glutamate 23 g. by mouth in the next two hours. Next morning (ten hours later) she was alert and had lost her abnormal neurological signs. This improvement was not well maintained, and a maintenance dose of sodium glutamate 23 g. by mouth daily became necessary. However, after a further four days the abnormal neurological signs returned and she became comatose. Sodium glutamate 30 g. was given intravenously, and she became rousable and able to answer simple questions. Treatment was discontinued because it was now clear that it could produce no lasting benefit, and the patient died thirty six hours later in deep coma. Necropsy was refused.

Case 5.—A man, aged 46 (case 1 of Walshe 1953), who also had chronic ulcerative colitis, had already had one episode of hepatic coma treated with sodium glutamate in 1952. Since that time he had kept in fair health until January, 1954, when, after an exacerbation of his colitis, he had a severe rectal hæmorrhage; he was admitted to hospital precomatose, with fœtor hepaticus and other signs of hepatic failure. Immediately after admission he was given a 3 pint blood transfusion, but his condition continued to deteriorate, and he became comatose. During the next twenty four hours he was given sodium glutamate 46 g. by slow intravenous infusion, and he had fully regained consciousness by the end of this time. He has remained in fair health during the following 9 months.

Case 6.—A woman, aged 30, was admitted in deep coma. She had apparently been unwell with nausea and vomiting for a month and had been jaundiced for two weeks. She had been in coma for about seventy two hours before her admission. She was deeply jaundiced, her liver dullness was reduced, her pupils were dilated, she was very restless, and ankle clonus and plantar responses were present. Treatment was directed to maintaining the fluid and electrolyte balances, and calories were supplied with 25% glucose solution; sodium glutamate 23 g. was given daily. There was no response to treatment, and the patient died on the third day.

At necropsy the liver was found to be severely necrotic; it weighed 800 g.

Case 7.—A woman, aged 45, with hepatic necrosis and fœtor hepaticus, was admitted in February, 1954. During the next ten days very careful control was kept of the fluid and electrolyte balance, calories were supplied by 25% glucose drip into the superior vena cava, and sodium glutamate 23 g. was given daily. After the first 23 g. of glutamate she could answer simple questions, but this improvement was not maintained, and there was no further apparent response to treatment before her death. For further details see Challenger and Walshe (1955b).

Summary.—4 new patients with chronic liver disease were treated with sodium glutamate,* either by mouth or intravenously, each for one or more episodes of hepatic coma or pre coma. 2 of them responded well. 1 of these left hospital in fair health to die later of mesenteric thrombosis, and the other had a good initial response but died later of hæmorrhage from œsophageal varices. The remaining 2 responded briefly only to die later of progressive liver failure. 1 of the 3 patients reported earlier (Walshe 1953) was treated in a second episode of coma and again responded. 2 cases of massive hepatic necrosis did not respond to treatment with glutamic acid.

Special Investigations

Metabolism of Amino acids

The metabolism of amino-acids was studied by paper chromatography in 2 cases of hepatic cirrhosis and in both cases of massive hepatic necrosis. In both cases of cirrhosis detailed studies showed a definite abnormality of the pattern of amino acids in the plasma during coma,

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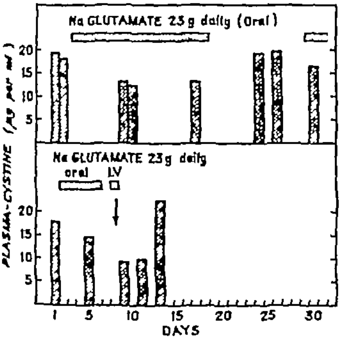
* When given intravenously either the monosodium salt of L (+) glutamic acid or a mixture of the sodium and potassium salts in the ratio 3 : 1 was used. When given orally either glutamic acid tablets 0·5 or a solution of monosodium glutamate was given in divided doses throughout the twenty four hours.



Plasma-cystine levels in two patients under treatment with glutamic acid.

most notable finding being the very high plasma thionine level. In the 2 cases of acute hepatic necrosis raised levels and disturbed pattern of the amino-acids the blood were more striking, here again the raised blood methionine level was the outstanding finding tamine was also detected in the plasma of one of the 3 patients. In 1 of these cases the cerebrospinal fluid (C.S.F.) showed very high levels of glutamine thionine and an unidentified ninhydrin colour reactor, sibly γ-aminobutyric acid Excess of tyrosine, phenyl nine, glutamic acid, and methionine sulphoxide was so detected.

The C.S.F. glutamine level has been studied in more tail by the method of Whitehead and Whittaker (1955) 15 healthy people it ranged from 6 to 16 mg r 100 ml (mean 10 mg per 100 ml.) A patient with rrhosis but not in coma had a C.S.F. glutamine level of 7 mg per 100 ml.; and another, who later became matose, 27 mg per 100 ml Of 3 patients studied while coma 1 had a C.S.F. glutamine level of 40 mg per 100 l. on oral glutamic acid and 41 mg per 100 ml. after was discontinued; another had 41 5 mg per 100 ml. fore treatment and 44 5 mg per 100 ml while on travenous glutamate and the 3rd had 45 mg per 0 ml. These results confirm the chromatographic ndings of a very high C.S.F. glutamine level in hepatic ma but suggest that glutamic acid therapy does not se this level still further

The metabolism of cystine and cysteine has been studied y polarography The plasma-cystine level is often ced in severe chronic liver disease (Walshe and Senior 55). In view of Christensen's (1949) finding that rge doses of oral glutamic acid depress the level of other sma-amino-acids in dogs the plasma cystine levels re studied in 2 patients, and the results (see figure) gest that the plasma-cystine level may be depressed y large doses of glutamic acid The normal plasma stine level estimated by this method is 6–14 µg per 0 ml. with a mean of 10 64 µg per 100 ml (Dent et al 54) and the figure shows that this range was much ceeded in both cases studied

BLE I—BLOOD LEVELS OF KETO ACIDS IN HEALTHY PEOPLE AND PATIENTS WITH CHRONIC LIVER DISEASE

—	α Keto glutaric acid (µg per 100 g)		Pyruvic acid (µg per 100 g)		Aceto-acetic acid (µg per 100 g)	
	Range	Mean	Range	Mean	Range	Mean
11 healthy people	86–302	143	160–390	230	91–300	161
cirrhotics	147–187	161	270–312	317	141–367	238

Metabolism of Keto-acids

Disturbed metabolism of keto acids has been described in patients with liver disease (Amatuzio and Nesbitt 1950, Seligson et al 1952, Amatuzio et al. 1952, Smith et al 1953) α Ketoglutaric acid links the metabolism of amino acids with that of carbohydrates: glutamic acid ⇄ α ketoglutaric acid + ammonia (Weil Malherbe 1936); either disturbances of intermediary carbohydrate metabolism or a failure of the ammonia binding action of glutamic acid might be reflected by a rise in the concentration of this keto acid

By the method of El Hawary and Thompson (1953) the levels of α ketoglutaric acid, pyruvic acid, and aceto acetic acid were determined in healthy people, in patients with chronic liver disease, and in patients in hepatic coma The results for the healthy people and the patients with chronic liver disease are given in table I It can be seen that whereas the average values for the patients with liver damage are higher than those of the healthy people, they remain within the range of normal variation The normal values given here agree well with those published by El Hawary and Thompson (1953) so far as the ketoglutarate and aceto acetate are concerned, but those for pyruvate are somewhat lower possibly owing to decomposition of this unstable compound during the lengthy process of extraction Oral doses of glutamic acid 10 g did not alter the blood ketoglutarate level in healthy people, nor did a rapid intravenous infusion of sodium glutamate 12 g much affect this fasting plasma ketoglutarate 106 µg per 100 g; after intravenous glutamate 125 µg per 100 g There was also no significant change in the levels of the other keto-acids This rapid glutamate infusion was much better tolerated by healthy persons than by patients with severe liver disease who may retch and salivate if the infusion is given too fast

TABLE II—BLOOD LEVELS OF KETO-ACIDS IN HEPATIC COMA IN A PATIENT WITH POST HEPATITIS CIRRHOSIS

Specimen no.	α Keto glutarate (µg per 100 g)	Pyruvate (µg per 100 g)	Aceto acetate (µg per 100 g)	Therapy and C.N.S. signs
1	300	583	406	No therapy precomatose state
2	314	720	635	8 hr after oral glutamate normal C.N.S.
3	364	350	445	2 hr after glutamate normal C.N.S.
4	437	537	314	No therapy terminal coma

TABLE III—BLOOD LEVELS OF KETO-ACIDS IN HEPATIC COMA IN A PATIENT WITH MASSIVE HEPATIC NECROSIS

Specimen no	α Keto-glutarate (µg per 100 g)	Pyruvate (µg per 100 g)	Aceto-acetate (µg per 100 g)	Therapy and C.N.S. signs
1	195	358	322	No therapy in coma
2	231	485	368	On I.V. glutamate and glucose coma
3	281	870	2420	On I.V. glucose only terminal coma

2 patients in hepatic coma were studied The 1st (case 4) had post hepatitis cirrhosis (table II)

The 2nd patient studied in hepatic coma was case 6 with massive hepatic necrosis (table III)

A single specimen of blood was obtained from a patient who had been in coma for more than a week after thrombosis of his portal and collateral veins; he was receiving 10% glucose intravenously at the time The blood ketoglutarate level was 338 µg per 100 ml., the pyruvate 1020 µg per 100 ml. and the aceto-acetate 455 µg per 100 ml †

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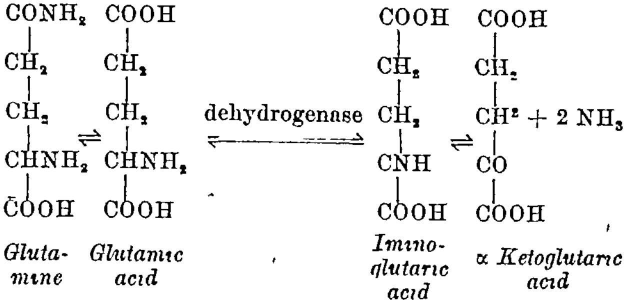
† Markees (19) suggests that the spot identified by El Hawary and Thompson (1953) as aceto-acetate may in fact be " pyruvate spot II " resulting from an isomer of pyruvic acid

Discussion

The present cases further support the theory that large doses of glutamic acid are sometimes of value in the treatment of coma in patients with hepatic cirrhosis The rôle of glutamic acid in the metabolism of the brain has been reviewed and discussed by Weil Malherbe (1952) Enzyme systems are present in the brain for the amidation, transamination, decarboxylation, and oxidation of glutamic acid In the ammonia binding mechanism glutamic acid probably enters the following reactions



$$\underset{\text{Glutamine}}{\begin{array}{c}CONH_2\\|\\CH_2\\|\\CH_2\\|\\CHNH_2\\|\\COOH\end{array}} \rightleftharpoons \underset{\text{Glutamic acid}}{\begin{array}{c}COOH\\|\\CH_2\\|\\CH_2\\|\\CHNH_2\\|\\COOH\end{array}} \xrightleftharpoons{\text{dehydrogenase}} \underset{\text{Imino-glutaric acid}}{\begin{array}{c}COOH\\|\\CH_2\\|\\CH_2\\|\\CNH\\|\\COOH\end{array}} \rightleftharpoons \underset{\alpha\text{ Ketoglutaric acid}}{\begin{array}{c}COOH\\|\\CH_2\\|\\CH_2\\|\\CO\\|\\COOH\end{array}} + 2\,NH_3$$

Thus an excess of intracellular ammonia will lead to a shift to the left in these reactions, with a consequent reduction in the supply of 4 carbon acids for the citric acid cycle This in turn would give rise to a switch in pyruvate metabolism to the formation of aceto acetate The necessary supply of ketoglutarate could be maintained by pyruvate and oxalo acetate accepting amino groups from glutamic acid, thereby permitting normal functions of both the Krebs cycle and the ammonia binding mechanism The high concentration of glutamic-acid decarboxylase in the brain probably mediates the reaction glutamic acid ⇌ α aminobutyric acid + CO_2 The escape of the resultant CO_2 would lead to a reduction in acidity and the freeing of fixed base Finally, glutamic acid carries the K^+ ion into the cell, probably as the preferential cation associated with the glutamic-acid anion (Terner et al 1950)

All the more recent workers in this field have assumed, without further evidence, that the importance of glutamic acid in hepatic coma lies in its key rôle in the ammonia-binding mechanism Riddell and McDermott (1954) show that, in patients in hepatic coma, the blood-"ammonia" level fell after the intravenous infusion of glutamic acid, a temporary fall was observed by Sherlock et al (1954), and the diagrams of Singh et al (1954) also appear to illustrate this, although these workers interpret their results otherwise The present biochemical studies throw no further light on the underlying metabolic disturbances No consistent changes were found in the blood levels of the amino acids, although the blood-methionine level was often raised The metabolism of keto acids also appeared to be disturbed, but intravenous glutamic acid did not much raise the blood-ketoglutarate levels, nor did the blood level of aceto-acetate rise consistently as might have been expected if the supply of 4-carbon acids for the citric-acid cycle had been reduced seriously by a disturbance of the ketoglutarate ⇌ iminoglutarate equilibrium in favour of the latter (cf Weil-Malherbe 1952) Moreover other factors, such as starvation and glucose loading, must have played a part in the high blood-levels of aceto-acetate and pyruvate which were found on occasions Bessman and Bessman (1954) believe that the toxic action of ammonia is the removal of ketoglutarate from the Krebs cycle, but they did not allow for the replacement from glutamic acid by the transamination reaction described by Weil Malherbe (1952)

In all the present cases where it was estimated the C S F-glutamine level was raised to approximately the intracellular level of glutamine but was not raised further by glutamic acid therapy, a finding which has also been reported by Whitehead and Whittaker (1955) This could be due either to a leakage of glutamine from the damaged cortical neurones or a compensatory mechanism to remove excess ammonia bound by the intracellular enzyme systems Such an enzyme system might then become exhausted, in the presence of severe liver disease, or blocked by some glutamic-acid antimetabolite (Walshe 1951), and failure to detect consistent changes in the blood level of either "ammonia" or keto acids would not eliminate the possibility that a deranged ammonia metabolism is important in the genesis of hepatic coma The undoubted fact that both oral ammonium salts and a high protein diet given to patients with severe liver damage can produce a syndrome closely mimicking hepatic coma further supports the theory that disturbed ammonia metabolism is in some way connected with the naturally occurring syndrome, but does not mean that it is the only cause of hepatic coma Indeed, Seegmiller et al (1954) have achieved very high blood "ammonia" levels (1 8 mg per 100 ml) without producing abnormal neurological signs, and Benitez et al (1954) note that the direct application of ammonium salts to the cortex did not give rise to altered cortical electrical activity, but they did find that the brain ammonia-level rose in fluoro acetate poisoning without a corresponding rise in the blood ammonia level Under the experimental conditions the cerebral ammonia was not readily converted to glutamine It has also been shown that the brain-ammonia level rises after electrically and chemically induced convulsions and in anoxia (Waelsch 1951) In severe hepatic disease, therefore, when the ammonia binding mechanism remains intact, a relatively high blood ammonia level could, at least in theory, be well tolerated, whereas in cases where some inhibiting factor was present a normal or only slightly raised blood ammonia level might exist coincidentally with a toxic level in the cortical neurones This could account for the conflicting evidence reported by many workers on the correlation of neurological signs with the blood ammonia levels It should perhaps be mentioned at this stage that the assumption that ammonia, in the concentrations reported, has a direct toxic action on th brain is not entirely supported by the available exper mental evidence, for, apart from the work of Benit et al (1954), Terner et al (1950) found that, althoug 0 005 *M* ammonia, a concentration many times great than that found in hepatic coma, caused a fall in th tissue potassium level it did not inhibit the uptake oxygen by brain slices Similarly, it has been reporte by Edson (1935) that the metabolism of brain slices in glucose medium is not inhibited by a 0 01 *M* concentration of NH_4Cl, a concentration which will reduce th respiration of the liver by 20%

It is not generally realised that the administration o methionine to patients with advanced liver disease ma be followed by coma This was first noted by Watso (1949), and more recently by Sherlock et al (1954 studying the toxic effects of nitrogenous compound in patients with portal hypertension The possibl mechanisms are discussed by Challenger and Walshe (1955a and b)

In an organ mediating as many complex metabolic pathways as does the liver it is unlikely that any single cause underlies all cases of hepatic coma In acute hepatic necrosis there is, in addition to a disturbed or destroyed hepatic function, the element of intoxication from the rapid necrosis and autolysis of hepatic parenchymal cells In hepatic cirrhosis two factors need consideration (1) in many cases there is a progressive loss of liver cells together with impaired function of the survivors, which must inevitably lead to a stage at which the liver can no longer support life, in chronic alcoholics, moreover, the picture is further complicated by damage to the nervous system by multiple enzyme deficiencies, and (?) in cases with chronic liver damage some precipitating factor, such as hæmorrhage, will precede the onset of coma, and it is in these cases only that therapy can hope to produce a temporary recovery, it is in this group that glutamic acid may prove of value.

Summary and Conclusions

The results obtained with intravenous sodium (or sodium and potassium) glutamate in the treatment of hepatic coma are reported 5 patients with chronic liver disease were each treated for one or more episodes of coma: 3 responded favourably but 1 died shortly after of massive gastro intestinal bleeding and 2 responded only partially and died later of progressive hepatic failure

2 cases of massive hepatic necrosis showed no response to treatment.

The rôle of ammonia in the pathogenesis of hepatic coma is discussed. The integrity of the intracellular ammonia binding mechanisms is probably more important than the plasma-ammonia level A high blood ammonia level may be well tolerated in those cases of liver disease in which the ammonia binding mechanism remains intact, and disturbances of this function may lead to the development of coma even before the blood ammonia level rises.

Certain disturbances of sulphur metabolism in hepatic coma are described. Large oral doses of methionine may precipitate coma Some possible toxic actions of methionine and closely allied compounds, referred to by Challenger and Walshe (1955b) are described

There is probably no single cause of hepatic coma common to all cases, and it would probably be more accurate to refer to 'the hepatic comas.

I wish to thank the Royal Society for a full time research grant, the Stothert research fellowship Prof M. L. Rosenheim for his advice and encouragement and for his and Dr. J D Nabarro s permission to study their cases.

REFERENCES

dulo D S., Nesbitt, S (1950) *J clin Invest* 29 1486
— Shifter N, Stutzman F L. Nesbitt, S. (1952) *Ibid*, 31 751
den, D., Pacheldt, G R., Stone W E. (1954) *Amer J Physiol.* 176 488
man, S. P Bessman A. N (1954) *Lancet* ii 335
— Fazekas, J F, Bessman A. N (1954) *Proc Soc exp Biol. N.Y.* 85 66
bert, R. J, Smith, E Werren J P (1954) *Gastroenterology* 26 650
llenger F Walshe, J M. (1955a) *Biochem J* 59 372
— — (1955b) *Lancet* i, 1239
nstein, H N (1949) *Biochem. J* 44 333
dson, C. S. (1954) *Amer J Med* 16 863
t, C. E., Senior, B., Walshe J M. (1954) *J clin Invest* 33 1216
L. (1935) *Biochem J* 29 [illegible]
Hervey M. F S Thompson R. H S (1953) *Ibid* 53 340
H. (1923) *Klin Wschr* 12, 1364
G J jun., Phillips, G B Davidson C S (195[illegible]) *New Engl J Med* 246 124
Dermott W V jun., Adams, R. D (1954) *J clin Invest* 33 1
S. (1954) *Biochem. J* 56, 703
W. M. Whitehead T P Whittaker S. R. F (1953) *Lancet* i, 1 [illegible]
L G., McDermott W V (1954) *Ibid* i 1203
M. H (1943) *Proc Soc exp Biol N Y* 52, 334
R., Phillips G B, Gabuzda, G J Davidson, C S (1953) *J Lab clin Med*, 42 492
J E., Schwartz R., Davidson C S (1954) *J clin Invest*. 33, 964
D McCormick, G J., Sborov, V (1952) *Ibid* 31, 661
H. Summerskill W H J White L P Phear E. A (1954) *Lancet*, ii 453.
L D., Barclay, J A Cooke, W T (1951) *Ibid*, i 1001
L H jun, Ettinger R. H Seligson D (1953) *J clin Invest* 32, 273.
C., Eggleston L V Krebs, H A (1950) *Biochem. J* 47 139
R P Gabuzda, G J jun. Ballou A N Davidson, C. S. (1954) *Metabolism*, 3 99
Caulert C., Devillier C Halff, M (1933) *Pr méd* 41 217
H (1951) *In* Anson M. L, Edsall, J T., Bailey K. *Advances in Protein Chemistry* New York vol vi
R. V (1951) *Lancet* i 157
J M (1951) *Quart J Med* 20 121
— (1953) *Lancet* i, 107
— Senior B (1955) *J clin Invest* 34 30
J (1949) *Ann intern Med* 31, 405
H (1938) *Biochem J* 30 663
— (1952) *Biochem. Soc Symposia* no 8, 1 18
T L., Whittaker S R. F (1955) *J clin Path* 8 81
— Prior A L (1954) *Lancet* ii 43

FŒTOR HEPATICUS

F CHALLENGER
D.Sc. Birm. F.R.I C
EMERITUS PROFESSOR OF ORGANIC CHEMISTRY IN THE UNIVERSITY OF LEEDS

J M. WALSHE
M.A M.B Camb M R C.P

From the Department of Colour Chemistry University of Leeds and the Medical Unit University College Hospital London

THE breath of patients with severe parenchymal liver disease often has a characteristic odour, fœtor hepaticus, which has been described as a musty smell (Schiff 1946) 'the smell of a freshly opened corpse" (Himsworth 1947), and 'a mixture of rotten eggs and garlic' (Davidson 1949) The smell may be only just detectable or so strong as to fill the room and has been considered to be due to indol or to an amine (Lichtman 1949)

Attempts to isolate from the breath the compound producing the fœtor have failed because of the very small quantities involved and the difficulty of getting a seriously ill patient to breathe against the resistance of a collecting system From the smell Davidson believed it to be a mercaptan, possibly derived from methionine or from cystine but not necessarily dependent on methionine therapy

In patients with a strong oral fœtor a very similar smell may be present in the urine Butt and Mason (1954) believed that the compound producing fœtor hepaticus was also present in normal urine and from 75 gallons of normal urine they isolated 6 mg of a compound which they believed to be a cyclic amine with nitrogen in the ring This was lost during recrystallisation and a further extraction of 100 gallons of normal urine gave no significant yield

We have studied the urine of a patient with massive hepatic necrosis and a strong fœtor in her breath and urine.

Case-report

A housewife aged 45 was admitted to University College Hospital with jaundice and in light coma. Her illness had started six weeks previously (in December, 1953) with anorexia, diarrhœa, and nausea; after a few days she became jaundiced but did not take to her bed and after a short illness she appeared to recover A month later jaundice returned this time with severe vomiting and prostration. She was admitted in February 1954 to another hospital and treated with aureomycin for infective hepatitis; but her condition continued to deteriorate fœtor hepaticus was noted and she became delirious and lapsed into coma with extensor plantar responses and ankle clonus. At this stage she was transferred to University College Hospital. Her course was progressively downhill and she died nine days later despite treatment with 25% glucose intravenously, careful control of fluid and electrolyte balance and intravenous sodium glutamate No amino acid supplements were given. During this time her urine had a strong fœtor similar to that in the breath but rather more offensive; this was present as soon as the urine was passed and was not due to infection or to decomposition on standing Paper-chromatographic study of the plasma showed a moderate generalised increase of all amino-acids commonly present and a great increase of methionine

Necropsy (Dr R A. B Drury) showed extensive necrosis of the liver which weighed only 840 g this reduction being due to almost complete destruction of the parenchymal cells

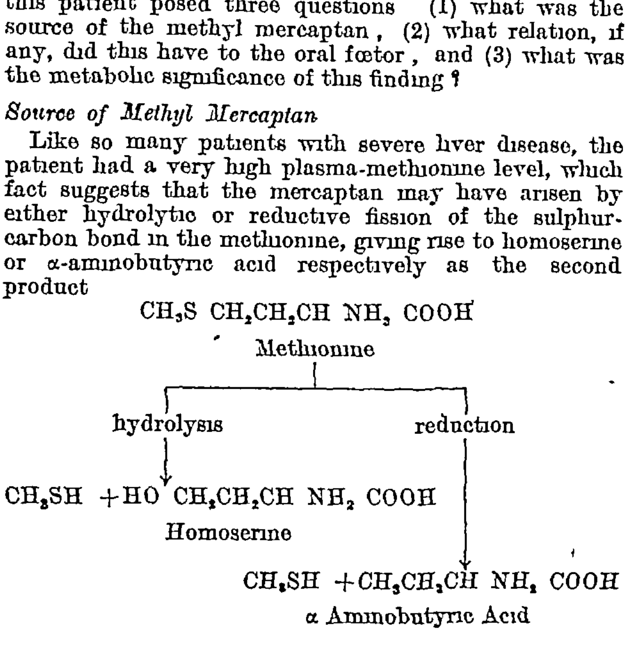
Examination of urine—The smell of the urine suggested that the compound responsible was either an alkyl mercaptan $C_nH_{2n+1}SH$ an alkyl sulphide $(C_nH_{2n+1})_2S$ or a dialkyl disulphide $C_nH_{2n+1}S\cdot S\cdot C_nH_{2n+1}$ or possibly all three We tried to isolate the responsible compound by bubbling a slow stream of nitrogen through 5 or 6 litres of urine next through dilute sulphuric acid (to remove ammonia) next through dilute mercuric cyanide and next through dilute mercuric chloride—a method evolved by Challenger and Rawlings (1937) and Blackburn and Challenger (1938) Details of the experimental procedure and the evidence for th chemical identification of the compounds isolated from the urine of this patient are described elsewhere (Challenger and Walshe 1955) The evidence obtained by this procedure showed that the urine contained methyl mercaptan (CH_3SH) as the principal compound producing the smell, and a smaller amount of dimethyl disulphide ($CH_3S\ SCH_3$), which may have resulted from oxidation of the methyl mercaptan after the urine was passed, there was no evidence for the presence of dimethyl sulphide in the urine

Discussion

The finding of methyl mercaptan, and probably dimethyl disulphide in smaller amounts, in the urine of this patient posed three questions (1) what was the source of the methyl mercaptan, (2) what relation, if any, did this have to the oral fœtor, and (3) what was the metabolic significance of this finding ?

Source of Methyl Mercaptan

Like so many patients with severe liver disease, the patient had a very high plasma-methionine level, which fact suggests that the mercaptan may have arisen by either hydrolytic or reductive fission of the sulphur-carbon bond in the methionine, giving rise to homoserine or α-aminobutyric acid respectively as the second product


$CH_3S\ CH_2CH_2CH\ NH_2\ COOH$
Methionine
hydrolysis
reduction
$CH_3SH\ +HO\ CH_2CH_2CH\ NH_2\ COOH$
Homoserine
$CH_3SH\ +CH_3CH_2CH\ NH_2\ COOH$
α Aminobutyric Acid

Such a fission, with the liberation of methyl mercaptan from methionine and S methylcysteine, is brought about by the mould *Scopulariopsis brevicaulis* (Challenger and Charlton 1947) The enzyme thionase occurring in liver (Binkley 1950), liberates methyl mercaptan from S methyl cysteine, $CH_3\ S\ CH_2\ CH\ NH_2\ COOH$ Its behaviour with methionine is not recorded Canellakis and Tarver (1953) report the formation of methyl mercaptan from methionine by rat-liver mitochondria

Normally the fate of methionine in the body, apart from being incorporated into protein, is to act as a source of cysteine and of labile methyl groups for the biological synthesis of choline, adrenaline, creatine, carnosine, and N-methyl-nicotinamide Probably many of these transmethylations occur in the liver and in cases of severe hepatic disease may be inhibited, with a consequent accumulation of methionine in the plasma, as happened in this patient Fission of the sulphur carbon link, with the formation of methyl mercaptan, may then be used as an alternative pathway to deal with the excess of methionine Evidence for this fission has also been obtained by Dent (1947), who found in healthy people and, especially, in a case of the Fanconi syndrome with hepatic cirrhosis an increased excretion of α-amino-butyric acid after the administration of methionine, " as if direct desulphurisation had taken place "

Relation to Oral Fœtor

In considering the relation of the methyl mercaptan in the urine to the oral fœtor it should be pointed out that this compound has a more offensive smell than is commonly associated with classical fœtor hepaticus Moreover, methyl mercaptan is relatively soluble, and the urine would be the natural route of its excretion However, dimethyl disulphide and methyl sulphide have an odour very like the sweetish oral fœtor Since the smell of these compounds can be detected in dilution of 10^{-7}, it can easily be realised how difficult would be to identify chemically such substances in th breath Moreover, if methyl mercaptan is present in th body, it is more than likely that at least a small proportion would be either methylated to dimethyl sulphid or oxidised to the disulphide The odour of garlic, whic has been likened to that of fœtor hepaticus, is due t diallyl disulphide ($(CH_2\ CH\ CH_2\ S-)_2$ Probably th smell of fœtor hepaticus is due to a mixture of dimethy disulphide, dimethyl sulphide, and methyl mercaptan possibly the proportions of each may vary in differen patients, explaining the differences in smell described b various observers

Metabolic Significance

Finally, are these findings of metabolic significance o of purely academic interest ? The finding of thiol group in the urine appears most surprising in view of the spee with which cysteine is oxidised to cystine in the blood It is perhaps a comparable finding to that of Walshe an Senior (1955) that patients with severe liver diseas cannot clear the blood of cysteine as fast as can health people The failure to convert the mercaptan to detectable amounts of dimethyl sulphide also points to seve impairment of methylation in the liver

The inability of the patient to metabolise methioni at the normal rate may also be of significance Ear et al (1942) showed that, when more than 6% of methionine is added to a low protein diet rats develop liv atrophy with a high mortality in one week Hepat coma has also developed in patients with severe liv damage when methionine has been given (Watson 194 Sherlock et al 1954) This action of methionine has bee attributed to the amino group, but the evidence is n entirely convincing Methionine itself is not necessari toxic, but perhaps some related intermediate metaboli may also accumulate Methionine sulphoxide is glutamic acid antimetabolite to *Lactobacillus arabino* (Waelsch et al 1946, Borek et al 1946) and so, theoretically, could inhibit the utilisation of glutamic acid in th brain Methionine sulphoximine, the toxic factor agenised flour, produces fits in dogs, an action that may reversed by glutamine (Bentley et al 1950, Heathcote an Pace 1950), a compound which it resembles structurall Is methyl mercaptan itself toxic ? We have been unab to find any evidence on this in published reports, b analogy with two closely related compounds suggests th it may well be so, there is clearly a close structural a chemical relationship between methyl mercaptan (CH_3SH and hydrogen sulphide (HSH) and methyl alcoh (CH_3OH) Hydrogen sulphide, in comparable concentrations, is as toxic as cyanide and interferes with th cytochrome system, and methyl alcohol is, as is we known, poisonous to the central nervous system Robert and Eckstein (1944) have found that dimethyl disulphi is toxic to rats in a dose of 90 mg per kg of body weig and then appears to yield methyl mercaptan. There no information about dimethyl sulphide, but this compound is a thio ether and so may well be toxic also

Summary

Methyl mercaptan was isolated from the urine of patient with massive hepatic necrosis, some dimeth disulphide was probably also present

It might be expected that, in the body, meth mercaptan would be either oxidised to dimethyl disulphide or methylated to dimethyl sulphide

We believe that fœtor hepaticus is caused by the elimination of one or more of these compounds in the breath

Little is known of the pharmacology of these compounds, but by analogy with closely related compounds they may well be toxic

We wish to thank Prof M L Rosenheim for permission to study this patient F C thanks Prof W Bradley for the hospitality of his department and J M W is indebted to the Royal Society for a whole time grant the Stothert research fellowship

REFERENCES

Bodley H R, McDermott E E Pace J Whitehead J K Moran, T (1950) *Nature Lond* 165 150
Dakhy I (1950) *J biol Chem.* 186 287
Blackburn, S., Challenger F (1938) *J chem. Soc* p 1872
Borek, F., Miller H K Sheiness, P Waelsch H (1946) *J biol Chem.* 163 347
Butt, H. R., Mason, H L. (1954) *Gastroenterology* 26 850
Dreifuss, L. S. Tarver H (1953) *Arch. Biochem. Biophys* 42 247 446
Challenger F., Charlton, P T (1947) *J chem. Soc* p 424
— Rawlings, A R. (1937) *Ibid* p 868
— Walshe J M. (1955) *Biochem. J* 59 372
Davidson, L S P (1949) *Lancet* ii, 197
Dent, C E. (1947) *Biochem. J* 41, 240
Dick D P, Small, K. Victor J (1949) *J exp Med* 76 317
Fantoni, J G, Pace J (1950) *Nature Lond* 166 353
Himsworth, H P (1947) Lectures on the Liver and its Diseases. 1st ed., Oxford.
Sherlock, S S. (1940) Diseases of the Liver Gallbladder and Bile Duct 2nd ed., London.
Lerra E., Eckstein, H C (1944) *J biol. Chem.* 154 367
Lutz L. (1916) The Differential Diagnosis of Jaundice Chicago
Sherlock, S., Summerskill W H J White L. P., Phear E A (1954) *Lancet*, ii 453
Waelsch, H Owades P Miller H K. Borek, E (1946) *J biol Chem.* 166 273
Walshe J M. Senior B (1955) *J clin Invest.* 34, 302
Wilson, C J (1940) *Ann. intern. med.* 31 405

THE TREATMENT OF ECLAMPSIA (IMMINENT OR ACTUAL) BY CONTINUOUS CONDUCTION ANALGESIA

R Bryce-Smith
M.A B.M. Oxfd., F.F.A.R.C.S
ASSISTANT NUFFIELD DEPARTMENT OF ANÆSTHETICS, OXFORD

E O Williams
M.A., B.M Oxfd, F.R.C.S M.R.C.O.G
CONSULTANT OBSTETRICIAN AND GYNÆCOLOGIST GUILDFORD SURREY

In 1947 a method of treating eclampsia by continuous conduction block was described by Hingson et al This followed the observations of Sarnoff and Farr (1944) that a single-dose spinal block was beneficial in hypertensive heart failure, and the realisation that spinal or extradural analgesia offered many advantages in the relief of pain during labour for patients handicapped by either cardiac or respiratory disease (Pitkin and McCormack 1928 Cosgrove et al 1937 Hingson and Edwards 1943)

At different times spinal analgesia has been strongly advocated for obstetric operations in toxæmic and eclamptic patients, but we believe that it was used therapeutically for the first time in 1928 (Paramore 1928) The introduction of methods which allowed conduction blocks to be maintained for long periods (Lemmon 1940 Hingson and Edwards 1942) greatly added to the practical value of this approach in the management of eclampsia. In this way it is possible to produce a controllable fall in blood pressure for any required length of time thus reducing the load on an embarrassed heart and avoiding the dangers of fœtal sedation

The first case to be treated thus in the United Kingdom was described by Bryce Smith et al (1949) Since then we have treated six more cases and in the light of this experience we have some further observations to make

Case reports

Case 1 —A primigravida aged 21 had a normal antenatal history until the 31st week, after which the blood pressure rose steadily œdema of the legs and albuminuria appeared and she was delivered of a stillborn child at the 35th week. After this she was admitted to this hospital as an emergency with a blood pressure of 170/100 mm Hg generalised œdema uræmia, anuria headache and disturbance of vision For the next twenty four hours during which she was sedated heavily the blood pressure continued to rise and the signs of cerebral irritation increased

A continuous caudal block was started but had little effect on the blood pressure despite apparently satisfactory high levels of analgesia (fig 1) The patient said she felt more comfortable but after twenty four hours she was becoming unmanageable and it was feared that she would pass into acute heart failure

A continuous spinal block was therefore established and her general condition much improved; the blood pressure was controlled (fig 2) and the cerebral symptoms vanished. During the ensuing thirty six hours there was a steady increase in urinary output (fig 3) with a corresponding reduction of œdema. The block was maintained for five and a half days, and only minimal sedation was necessary to maintain the required restful state The patient made such good progress that the catheter was removed but four days later finding restrictions of her activity irksome she got out of bed while unattended for a moment, collapsed and died of acute heart-failure

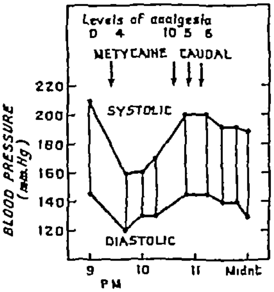


Fig 1—Case 1: Apart from an initial fall following the establishment of the caudal block the blood-pressure remained high in spite of adequate levels of analgesia.

Case 2 —A primigravida, aged 34 was admitted to hospital as an emergency having had four eclamptic convulsions at home Her normal weight was 20 st. and she was not aware that she was pregnant although her uterus was enlarged to the size corresponding to a pregnancy of 36 weeks. At this time her weight was estimated at 26 st. She was breathless delirious and uncoöperative Her blood pressure was 280/220 mm. Hg and she had oliguria, albuminuria, and gross œdema. Heavy doses of sedatives administered for eighteen hours did not alter this picture

A continuous lumbar extradural block was instituted For four hours there appeared to be some reduction in the systolic blood pressure with a gradually falling pulse-rate Subsequently the blood pressure was not lowered effectively although an increased volume of solution was injected into the extradural space; and there was some doubt about whether the catheter was correctly situated

A continuous spinal block was therefore substituted which brought the blood pressure under immediate control (fig 4) with satisfactory improvement in the patient's general condition. The spinal block was maintained for three days, during which no sedatives were necessary and within twenty four hours the output of urine had returned to normal (fig 3)

Progress —The blood pressure tended to settle at 140/90 mm. Hg presumably the patient's normal level, and no attempt was made to reduce it further The patient went into spontaneous labour eighteen hours after the start of the spinal block and was delivered of a stillborn fœtus It was not known whether the fœtus was alive when the patient was admitted because it was impossible to detect the fœtal

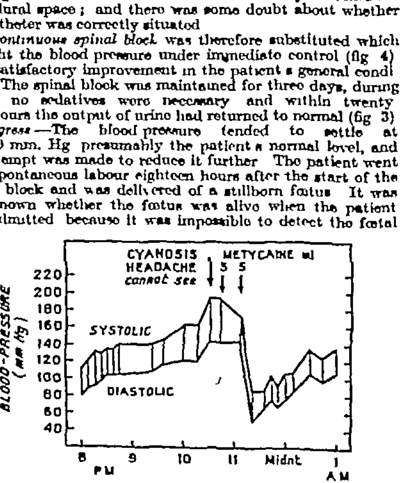


Fig 2—Case 1: dramatic effect of spinal analgesia on blood-pressure

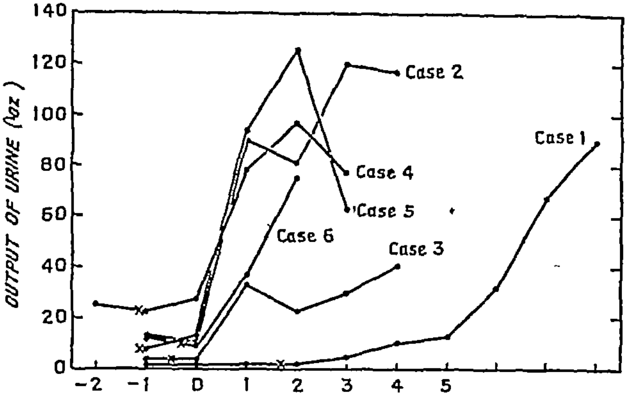


Fig 3—Daily urinary outputs of the six cases described : X, indicates time at which relevant blocks were established, and D the day of delivery Cases 1 and 3 suffered severe permanent renal damage, which probably accounts for their failure to conform to the pattern of post delivery diuresis seen in the other cases.

heart in the presence of such gross obesity When the catheter was to be removed from the subarachnoid space, a routine sample of cerebrospinal fluid (C S F) sent for examination showed infection with *Pseudomonas pyocyanea* This complication resulted from the incontinence of the patient and from the difficulties of nursing a paralysed woman of this weight The infection was overcome with massive intrathecal injections of streptomycin. There were no clinical signs of meningitis, and the patient made a full recovery with no signs of renal or cardiac damage

Case 3 —A primigravida, aged 21, who had received inadequate antenatal supervision, was admitted to hospital as an emergency at 28 weeks, having had three eclamptic convulsions at home On admission she was restless and uncoöperative, with a blood pressure of 190/150 mm Hg, albuminuria, and slight œdema Sedatives had little effect on the blood-pressure

A lumbar extradural block was instituted. The patient went into spontaneous labour and the blood pressure was efficiently controlled for about four hours, while labour progressed without disturbing the patient Thereafter, although increasing volumes of local analgesic solution were injected and had some effect, it became increasingly difficult to lower the blood pressure (fig 7) Restlessness increased, and it was discovered that the 'Polythene' tubing had broken at the skin margin. Rather than re-establish an extradural or spinal block through a potentially infected extradural space we reluctantly reverted to heavy sedation. Since the initial treatment had been ineffective, we were not surprised that this had little effect on the blood pressure, and the patient caused anxiety until she was delivered of a stillborn fœtus fourteen hours later The distal fragment of the polythene catheter was not removed at the time, and an attempt to locate it three weeks later was unsuccessful When seen a year later, the patient had not suffered on account of this, but she exhibited permanent and grave hypertensive damage to her kidneys and heart This case did not show a characteristic diuresis after delivery, and this is probably related to her permanent renal damage (fig 3)

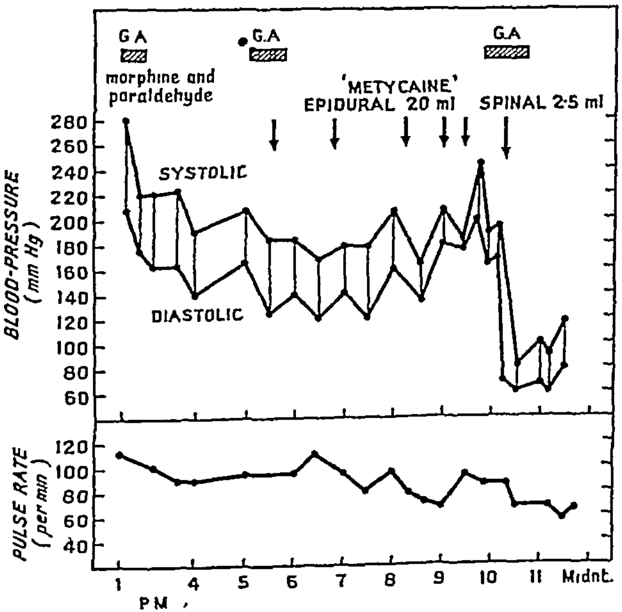


Fig 4—Case 2, showing effects of lumbar extradural and spinal blocks : G.A., general anæsthesia.

Case 4 —A primigravida, aged 19, was a booked case with a normal antenatal history until the 33rd week, when she had a raised blood pressure, albuminuria, and œdema of the face On admission to hospital next day the blood pressure had risen to 180/130 mm Hg and there was massive albuminuria Heavy sedation maintained for sixteen hours had no effect on the blood pressure

A continuous lumbar extradural block was instituted, and the patient was delivered spontaneously forty two hours later of a living baby weighing 4 lb During the period of continuous extradural block it was found that labour appeared to be retarded when the level of the block was raised to control the blood pressure adequately After thirty hours it became necessary to increase the volume of the local analgesic solution injected and to make the injections more frequently Thus at the beginning of the treatment 15 ml of 1% lignocaine was effective, but at the time of delivery 50–60 ml of solution was required to achieve the same effect (fig 8) The urinary output returned to normal rapidly (fig 3), and the patient made a satisfactory recovery

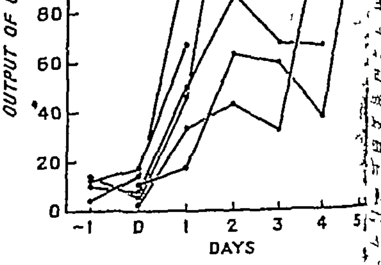


Fig 5—Daily urinary outputs of six eclam patients treated by heavy sedation.

Case 5 —A primigravida, aged 21, had a normal antenatal history until the 28th week, when the blood-pressure started to rise and œdema and albuminuria appeared At 36 weeks the patient was admitted to hospital as an emergen with a blood pressure of 200/140 mm Hg, generalised œdem drowsiness, and severe oliguria Sedation with morphine a paraldehyde maintained for six hours had little effect on t blood pressure

A continuous lumbar extradural block was instituted Uteri contractions were noticed at this time but ceased when t level of analgesia rose above T9 To control the blood pressu a higher level was required, and this presented difficulty witho interfering with labour After about twelve hours it beca necessary to increase the volume of solution injected a to make the injections more frequently Minimal sedati was required, and after twenty four hours the patient w delivered by forceps of a live baby Although analgesia w adequate for delivery, an acute hypertensive crisis develop immediately afterwards, and this could not be controlled b the block It became necessary to reinstitute heavy sedatio and within one or two hours the blood pressure had settled a the patient made an uninterrupted recovery with a satisfacto diuresis (fig 3) In retrospect we believe that the *conductio* block was started before sedation had been given a fair tri

Thus this case differs from the five others in whic sedation was fully exploited, and even then did not lowe the blood pressure A further point in this patient's history is worthy of interest when a rapid injection wa made through the extradural catheter, the patien complained of severe headache, persisting for about on minute, when the injection was made slowly this di not happen The ætiology of this phenomenon is discussed below

Case 6 —A multigravida aged 27 was admitted to hospital from the antenatal clinic at the 35th week with a raised blood pressure and albuminuria. For the next three days the blood-pressure continued to rise until it reached 220/140 mm. Hg despite treatment with diamorphine hydrochloride 'Sodium amytal' 'Serpasil,' and, later morphine and paraldehyde.

A lumbar extradural block was established under general anæsthesia, and the membranes were ruptured No further sedatives were given and the blood pressure was immediately controlled with extradural injections of 1% lignocaine and for several hours remained constant at 110/80 mm Hg—the patient's normal level. Strong uterine contractions were occurring regularly but for ten hours there was clinically little evidence of progress It then became necessary to give the extradural injections at shorter intervals, but despite this the blood pressure could not be maintained as steadily as before This led us to believe that labour was now progressing rapidly and she was delivered spontaneously three hours later of a living female child weighing 5½ lb

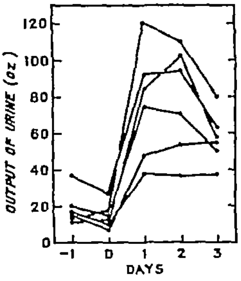


Fig 6—Daily urinary outputs of six healthy obstetric patients.

Sedation

To avoid repetition details of sedation have not been included in the case reports The routine adopted in all cases is the administration of heavy doses of sedatives to lower the blood pressure and to control convulsions. Where necessary a general anæsthetic may be given also to assess the patient obstetrically Thus, as an extreme example case 2 received a general anæsthetic, followed by rectal paraldehyde 21 ml in olive oil, intramuscular paraldehyde 10 ml morphine 32 mg., and sodium amytal 300 mg within ninety minutes Although convulsions ceased and her respirations decreased to 6 per minute her blood pressure was not controlled. If, however a satisfactory reduction of blood pressure is achieved it can generally be maintained by giving intramuscular morphine 16 mg, and rectal paraldehyde 21 ml (in 170 ml of olive oil) alternately every four hours

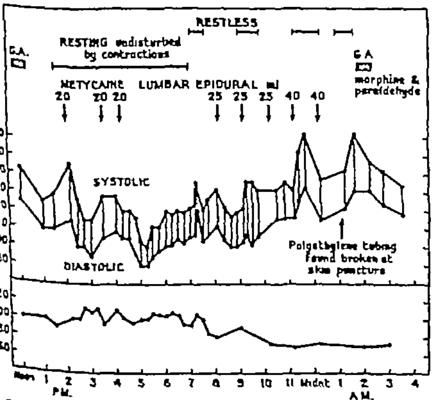


Fig. 7—Case 3 showing failure of what had been an effective extradural block owing to breakage of the polythene catheter: G.A., general anæsthesia.

Methods and Technique of Anæsthesia

In the six cases reported here, caudal, lumbar extradural and spinal approaches were used A length of plastic tubing was inserted through either a caudal or a Tuohy needle (Southworth et al. 1953) The site of puncture is sealed with paraffin gauze impregnated with penicillin powder, and the external part of the plastic tubing is fastened to the patient's back with a long length of adhesive strapping 2 inches wide The free end, to which a syringe remains attached can be either brought over the patient's shoulder and fixed to the chest or placed under a pillow

Since conduction blocks of this type may need to be maintained for several days at a time the risk of infection is obvious, and the utmost care is needed to avoid contamination of the free end of the plastic catheter To ensure this a syringe attached to the free end of the tubing provides, we believe, the most effective seal, but a fresh sterile syringe must be used for each injection When a continuous spinal block is in progress the pressure of C.S.F may force back the plunger of the syringe allowing it to become contaminated This can be avoided by strapping the plunger to the barrel of the syringe It is advisable to take routine samples of C.S.F so that if infection is introduced it may be recognised immediately and appropriate treatment instituted

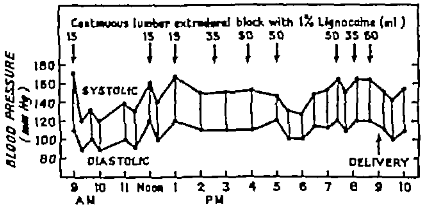


Fig 8—Case 4 showing control of the blood-pressure; it was necessary to increase progressively the volume of local analgesic solution injected into the extradural space and to make these injections at shorter intervals.

Since it is often difficult to achieve an adequate level of analgesia with a caudal block we believe that this approach is the least useful in the management of eclampsia Usually, a continuous caudal block used for delivery in normal obstetrics has little effect on the blood pressure (Lull and Hingson 1948) and this was so in case 1

A lumbar extradural block usually provides adequate levels of analgesia and efficient control of the blood pressure for limited periods. However in all the cases in which the method was used it was found that, with the passage of time, increasing volumes of solution were needed to obtain the desired result and that as the time for delivery approached the injections had to be given more frequently Also on some occasions it became impossible to provide a sufficient fall in blood pressure There is no doubt that a spinal block provides a far more efficient and certain method of controlling the blood pressure, but this technique carries with it the risk of meningitis.

Case 1 shows that violent swings of blood pressure can lead to heart failure whose warning signs are a falling pulse pressure and a rising pulse-rate (fig 9) If the blood pressure and pulse rate are charted graphically these signs are seen readily This method of recording also demonstrates the basic blood pressure level of each case, and no advantage is gained by lowering the blood pressure further (cases 2 and 6)

Before any of the blocks under discussion are undertaken, certain safety measures should be to hand—oxygen, a means of inflating the lungs, transfusion apparatus, a tilting bed, and a vasopressor drug such as methylamphetamine hydrochloride ('Methedrine') A syringe containing thiopentone is advisable, too, in view of the remote possibility of convulsions due to rapid absorption of the drug used for producing local analgesia

The injection of solution into the extradural space undoubtedly influences the pressure of the C S F, and this fact has been used in treating postspinal headaches (Rice and Dabbs 1950). However, we are not aware of any method which will raise the pressure of the C S.F in a healthy person to such an extent that headaches result Case 5 is exceptional in that a rapid injection of solution into the extradural space caused a violent headache lasting about a minute A slow injection did not have this effect This time relationship coincides closely with the duration of peak C S F pressures when these are raised by injection into the subarachnoid space (as during the induction of spinal analgesia) Experiments made by one of us (R B-S) showed that the intraspinal injection of 15 ml of light cinchocaine could raise a normal C S F pressure to about 650 mm H_2O, but the pressure fell rapidly to 150 mm H_2O within thirty seconds and then returned to the normal pre injection level much more slowly In these experiments the patients suffered no headaches, but it could be argued that in case 5 the C S F pressure was already raised by œdema of the brain

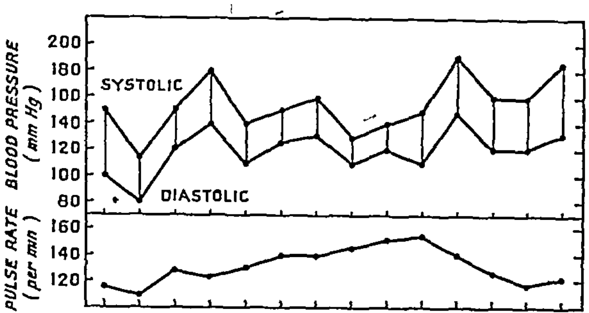


Fig 9—Case 1: In an effort to promote diuresis the blood pressure was made to "swing" During the period between 5 p m and 9 p m the pulse-pressure fell and the pulse-rate (indicated by the lowest line) rose, the patient tended to be slightly cyanosed, and her respiration became "bubbly" As the pulse-pressure increased, so the pulse-rate fell and the patient's general condition improved

Obstetric Problems

There seems to be little doubt that, once the blood pressure has been controlled by continuous conduction block, heavy sedation is unnecessary By controlling the blood-pressure it is possible to avoid eclamptic convulsions and the subjective symptoms of headache, disorientation, and blurred vision so commonly present in a hypertensive crisis

The avoidance of heavy sedation by using continuous conduction block offers the best chance of survival for the fœtus and tends to reduce the incidence of respiratory morbidity in the mother The comparison between the wide awake cooperative patient under conduction block and the comatose woman under heavy sedation, who, despite skilled nursing, is liable to develop pulmonary complications, is most striking The dangers in heavy sedation of balancing the claims of the fœtus against those of the mother, as the time of delivery approaches, can also be avoided Apart from its therapeutic value the block also serves as the anæsthetic for delivery, whether operative or spontaneous

In cases 4 and 5 there was evidence that the progress of labour was retarded by the block when it reached the level considered adequate for controlling the blood pressure It often requires fine judgment to choose the proper dosage which will provide a level of analgesia sufficient to control the blood pressure yet at the same time not interfere with the normal course of labour

We intend in future to maintain the block at the best level for controlling the blood-pressure and to use, when necessary, an oxytocin drip (1–5 units of oxytocin per 500 ml of 5% glucose solution according to individual response) to stimulate a normal rate of labour

Effect on Urinary Secretion

Hughes et al (1948) described dramatic responses i patients with oliguria and even anuria to continuou conduction blocks This was not seen in any of our case All, however, showed a striking diuresis followin delivery, which usually took place within twenty fou hours of establishing the block (fig 3) Daily urinar output charts of six eclamptic patients treated by heav sedation with morphine and paraldehyde (fig 5) and s healthy obstetric patients (fig 6) show a similar patter As might be expected, the daily output of the health patients was not usually so high as that of the eclampti patients, since excessive antenatal retention of fluid characteristic of the latter group

We have seen anuria from other causes respon favourably to block therapy, but in this series the post partum diuresis was related to the time of deliver an was uninfluenced by any therapeutic measures

Conclusions and Summary

Six cases of eclampsia treated by continuous conductio block are described Our present impression is that block by the caudal route is of little value The bloo pressure is controlled most effectively by continuo spinal analgesia, but this carries the risk of meningit A continuous lumbar extradural block is safer, and i twenty four hours will give almost as good results a spinal

Whichever method is chosen, there is a chance th labour will be retarded by a block which reaches t optimal level (varying from patient to patient) f controlling the blood pressure. In such instances, it suggested, rather than to lower the level of the block, pitocin drip should be established to stimulate norm uterine function

The improvement in the appearance of an eclampt patient treated with conduction analgesia is strikin and, since heavy sedation is unnecessary, matern morbidity is reduced and the fœtus offered better chan of survival

On these grounds a continuous conduction block i selected cases is preferable to treatment with sedatives but, since a postpartum diuresis can be expected t follow delivery in most cases, eclamptic oliguria by its does not necessarily provide a specific indication fo block therapy

At present we do not feel justified in suggesting th a conduction block be used in all cases of severe toxæmi but in desperate cases, such as we have described, bloc therapy has much to offer Nevertheless such treatmen presents a disadvantage, since it is necessary to provid constant supervision throughout the twenty four hour by an anæsthetist and an obstetrician, who must alwa be at hand

We are grateful to the nurses for their untiring help wit these cases, Sir Robert Macintosh for his valuable adv and assistance, and Mr J Stallworthy and Mr W Hawksworth, under whose care these patients were admitted to the United Oxford Hospitals, for their advice and permission to publish

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MUSCLE IMBALANCE IN THE CAUSATION OF SCOLIOSIS

H F V RIDDLE
B.Sc Lpool
RESEARCH ASSISTANT IN THE DEPARTMENT OF ANÆSTHESIA, UNIVERSITY OF LIVERPOOL

ROBERT ROAF
M.A., B.M Oxfd, M Ch Orth Lpool, F.R C.S
F.R C.S E   D Obst
LECTURER IN ORTHOPÆDIC SURGERY UNIVERSITY OF LIVERPOOL DIRECTOR OF CLINICAL STUDIES SHROPSHIRE ORTHOPÆDIC HOSPITAL, OSWESTRY

FUTURE progress in the prevention and treatment of deformities will largely depend on increasing our knowledge of their ætiology Although the conclusions of this paper are tentative and incomplete, we feel that they are worth recording because they throw light on a difficult and important problem—the ætiology of scoliosis.

In some cases of scoliosis there are obvious skeletal abnormalities—e.g, hemivertebræ, fused ribs, and funnel chest These are cases of congenital scoliosis

In other cases the scoliosis develops after an attack of poliomyelitis—so-called paralytic scoliosis Even in these cases, however the exact mechanism of production of the deformity is uncertain (Steindler 1929 Lowman [illegible], Mayer 1936 Colonna and Vom Saal 1941) If it is merely a question of muscle imbalance which muscles are concerned ? Spinal or extraspinal ? If spinal are the stronger muscles on the convex or the concave side ? It has been suggested that fascial contracture (Bennett [illegible]52, Clark 1954) may be responsible or that there is a primary disturbance of vertebral growth even in paralytic cases

Next there is a relatively small group of cases in which the scoliosis is associated with a condition such as muscle dystrophy neurofibromatosis syringomyelia or hereditary ataxia

Finally there is the largest group of cases in which no definite cause can be found for the scoliosis—the 'idiopathic' group

The object of the present investigation was to assess the rôle of muscle imbalance in scoliosis Known cases of paralytic scoliosis were examined to find out which muscles were weak and what type of imbalance caused deformity Next some cases of idiopathic scoliosis were examined to discover whether occult muscle imbalance (undetectable clinically) played a part in causing some of these deformities The theory that many cases of idiopathic scoliosis are due to an undiagnosed attack of poliomyelitis is, of course an old one but hitherto it has been hard to find objective evidence in support of this theory We also examined cases of congenital scoliosis to act as controls.

Methods

It is relatively easy to assess the strength of limb muscles clinically but it is difficult to assess the strength of individual trunk muscles by ordinary clinical means. Jansen (1913) suggested that unequal diaphragmatic activity was a cause of scoliosis Therefore we had radiographs taken of both sides of the diaphragm in full inspiration and full expiration, and measured their excursion The other trunk muscles were assessed by electromyography

A two channel electromyograph was used to compare the activity of muscles on each side of the body Recordings were usually made with surface electrodes but in some cases needle electrodes were also used for the deep spinal muscles

The electromyograms were displayed side by side on a double beam oscilloscope and their amplitudes compared The amplitudes are directly related to the mechanical response of the muscles (Inman et al 1944 Loofbourrow 1948) they were expressed as submultiples of a full scale deflection arbitrarily defined as 5 units

The procedure adopted was as follows When the patient was comfortable on a couch the skin over the *muscles to be investigated was carefully cleaned and* massaged with an electrode jelly saturated with salt. The electrodes were next placed at equal distances apart on either side A standard distance could not be adopted because of the deformities resulting from the scoliosis. The electrodes were securely fastened to the skin with adhesive tape and records were taken during certain standard procedures (1) maximal inspiration (2) maximal expiration (3) head raising (4) left lateral flexion of the trunk and (5) right lateral flexion of the trunk. The respective situations of the electrodes (normally two inches apart) were as follows (1) on the lateral abdominal muscles in the anterior axillary line (2) on the rectus abdominis muscle one inch from the median line

TABLE I—RESULTS OF ELECTROMYOGRAPHY IN TYPICAL IDIOPATHIC THORACIC SCOLIOSIS (CASE 30)

Muscle	Side	Inspiration	Expiration	Head raising	Right lateral flexion	Left lateral flexion	Total
Lateral abdominal	R	4	5	1	5	1	16
	L	5	5	2	1	5	18
Rectus abdominis	R	0	1	1	2	1	5
	L	0	½	1	1	1	3½
Intercostal	R	1	4	5	3	5	18
	L	4	4	5	2	0	15
Lumbar	R	0	0	5	3	5	13
	L	0	0	5	3	5	13
Lower thoracic	R	1	0	4	2	1	8
	L	2	0	5	1	1	9
Upper thoracic	R	1	0	3	3	1	8
	L	1	1	4	1	2	9
Needle electrodes at T9 level	R	4	0	5	4	4	17
	L	2	0	5	2	4	13

TABLE II—SUMMARIES OF SIX TYPICAL CASES

Muscle	Side	Case 30	Case 11	Case 19	Case 50	Case 16	Case 35
Lateral abdominal	R	15	7	6	11	14	9
	L	18	16	11	8	14	12
Rectus abdominis	R	5	5	/	10	11	7
	L	4	11*	/	9	10	8
Intercostal	R	18	19	/	9	7	17
	L	15	8	/	12	6	15
Lumbar	R	13	18	[illegible]	16	12	15
	L	13	10	9	15	11	14
Lower thoracic	R	8	9	14	16	14	17
	L	9	20	8	15	13	13
Upper thoracic	R	8	13	17	12	10*	16
	L	9	12		13	6	[illegible]
Needle at apex of curve	R	17	2	21	[illegible]	18	[illegible]
	L	13	22	2	18	3	4

* Difference considered significant

Cases 30 and 35 idiopathic cases 11 19 50 and 16 paralytic.

Cases 30 11 and 50 convex to left cases 19 16 and 35 convex to right

Cases 50 and 35 primary lumbar curves cases 30 11 19 and 16 thoracic

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DR. BRYCE SMITH MR WILLIAMS   REFERENCES

Bryce-Smith, R., Seward F H Williams E A Williams T O Madden, R A (1949) *Lancet* ii 531
Moore S. A., Hall, I O Gleeson W J (193) *Curr Res. Anesth.* 16 231
Brown, R. A., Edwards, W B (1942) *Ibid* 21 301
— — (1943) *J Amer med Ass* 123 538
Whitacre, F E., Hughes J G Turner H B Barnes H J G (194) *Southern Surgeon*, 13 580
[illegible] J G Lovejoy, G S Lynn H D Hingson R A (1945) *Amer J Dis Child* 75 491
[illegible], W T (1940) *Ann Surg* 111 141
[illegible] C. R., Hingson R A (1948) Control of Pain in Childbirth 3rd ed., Philadelphia p 120
[illegible] R H (1925) *Proc R Soc Med* 21 70
[illegible] McCormack I C. (19 8) *Surg Gynec Obstet* 47 713
[illegible] O., Dalbe [illegible] H (1950) *Anesthesiology* 11 17
[illegible] A., Farr H W (1944) *Ibid*, 5 69
[illegible] J L. Hingson R A Pitkin W M (1953) Pitkin's [illegible] Anesthesia, 2nd ed., Philadelphia

(3) on muscles in the sixth intercostal space in the midclavicular line, (4) on the superficial spinal muscles at equal distances (usually 1½ inches) on either side of the spinous processes and at three different levels, and (5) the deep spinal muscles were investigated by touching the laminæ with the needle point and withdrawing the needle about a quarter of an inch

Usually skin electrodes were used, but in addition, whenever possible, recordings were taken from the deep spinal muscles with needle electrodes This requires considerable coöperation from the patient, and needle electrodes cannot be easily used in small children Electromyography was also used for investigating muscle activity in a large number of healthy adults and gives an accurate picture of the electrical activity of the muscle fibres in the vicinity of the electrodes

The usual procedure has been to take recordings from both sides simultaneously during inspiration, expiration, head raising, and right and left lateral flexion of the trunk Thus in most patients about sixty recordings were made, and these were repeated, if necessary, until we were satisfied that we had obtained an accurate and consistent record

On each movement activity was assessed on an arbitrary scale of 0–5 The figures for each side were then added If the ratio between the sums of the figures for each side was less than 2 1, the difference was considered insignificant and activity was recorded as equal If the difference was greater than 2 1 it was considered significant

In tables III and IV "ipse" means that the muscles on the same side as the convexity of the major curve ar significantly stronger, and "contra" means that th muscles on the concave side are significantly stronger (0) indicates that the ratio was between 2 1 and 3 1 and (+) that the ratio was over 4 1, otherwise the was between 3 1 and 4 1

Although the numerical assessments are somewh arbitrary they were always done by the same observ (H F V R), who is experienced in electromyograph and did not know the clinical assessment of the patien The details of one typical investigation are set out table I, the summaries of six typical ones in table II, the summaries of all the recordings in table III, and th salient features in table IV For the sake of brevity an clarity only the recordings from the spinal muscles the apex of the major curve are recorded in table II although recordings were taken from at least three leve in nearly all the patients

TABLE III—SUMMARIES OF ALL CASES INVESTIGATED

Case no	Needle electrodes at apex	Surface electrodes at apex	Abdominal	Intercostal
Paralytic thoracic				
1		Ipse (+)	Ipse	Equal
2		Ipse	Equal	Equal
3		Equal	Contra (+)	Equal
4 *		Equal	Contra (0)	Equal
5		Ipse (+)	Contra	Ipse (0)
6		Ipse (0)	Ipse (+)	Ipse (0)
7 *		Equal	Equal	Equal
8		Equal	Equal	Equal
9 *		Equal	Equal	Contra (0)
10		Ipse	Ipse	Ipse
11	Ipse (+)	Ipse (0)	Contra	Ipse (0)
12	Ipse (+)	Ipse	Contra	
13		Ipse (+)		Ipse
14	Ipse	Equal	Ipse	Ipse
15	Ipse	Equal	Ipse	Contra
16	Ipse (+)	Ipse (+)	Equal	Equal
17	Ipse	Equal	Equal	Equal
18	Equal	Ipse (+)	Contra	Contra
19	Ipse (+)	Ipse (0)	Ipse	Ipse
20		Ipse (+)	Contra (0)	Equal
Idiopathic thoracic				
21		Ipse (+)	Equal	Ipse
22	Ipse (0)	Equal	Equal	Ipse
23		Ipse (0)	Equal	Contra (0)
24		Ipse (0)	Ipse	Contra
25	Ipse (+)	Equal	Equal	Equal
26	Equal	Equal	Ipse (+)	Ipse (+)
27	Ipse (+)	Ipse (0)	Equal	Ipse (0)
28		Ipse	Equal	Ipse
29	Ipse (+)	Ipse	Equal	Ipse
30	Equal	Equal	Equal	Equal
31	Ipse (+)	Equal	Ipse	Ipse
32	Ipse (+)	Equal	Equal	Ipse
33	Equal	Equal	Contra	Equal
34		Ipse (0)	Equal	Equal
35	Ipse (+)	Ipse (0)	Equal	Equal
36		Ipse	Equal	Equal
37	Ipse (+)	Ipse	Contra (0)	Ipse
38	Ipse	Equal	Equal	Equal
Congenital thoracic				
39		Equal	Equal	Equal
40		Ipse	Equal	Equal
41		Ipse	Contra	Ipse
42 †	Ipse	Ipse (+)	Equal	Ipse
43		Ipse (0)	Equal	Equal
44		Ipse	Contra	Ipse
45	Contra	Contra (0)	Equal	Contra (0)
46		Equal	Equal	Equal
47	Ipse	Contra	Ipse	Ipse
48		Equal	Equal	Equal
49		Equal	Equal	Equal
Lumbar paralytic				
50	Ipse (+)	Equal	Ipse (0)	Ipse (0)
51		Equal	Equal	Ipse (0)
52		Ipse (+)	Ipse	Equal
53		Ipse (+)	Ipse	Equal
54		Ipse (0)	Ipse	Ipse
55		Contra	Equal	Equal
56	Contra (0)	Ipse (+)	Ipse	Ipse
57		Equal	Contra (+)	Ipse
Lumbar idiopathic				
58	Ipse (+)	*Ipse (0)*	*Contra (0)*	*Contra (0)*
Lumbar spasmodic				
59‡	Contra (+)	Contra (+)	Contra (+)	Contra (+)

* Only slight deformity

† Neurofibromatosis

‡ Case 59 is perhaps not strictly comparable to the others in that he was an adult, the cause of the scoliosis was an acute spasm which disappeared under anæsthesia, and it was a pure lateral flexion with little rotation It is included because the mechanism of production of the scoliosis contrasts with what was found in most of the other cases It illustrates what one would expect—i e, that scoliosis can be produced in more than one way

Ipse the muscles on the same side as the convexity of the curve are stronger *Contra* the muscles on the opposite side to the convexity of the curve are stronger

(0) Ratio between 2 1 and 3 1 (+) Ratio of more than 4 1
Remaining ratios between 3 1 and 4 1

Results

In 57 of 59 patients examined no significant asymmet of diaphragmatic excursion was observed In the others diaphragmatic herniæ were associated wi congenital scoliosis

The results of electromyography of intercostal, abdom nal, and spinal muscles are expressed in tables III and I

No significant correlation was found between imbalan of intercostal and abdominal muscles and the directi of deformity

In 15 out of 20 cases of paralytic thoracic scoliosis and 4 out of 8 cases of paralytic lumbar scoliosis the muscles the apex of the curve were significantly stronger on th convex side (often many times as strong as those on th other side) Of the remaining 9 cases the muscles we equal in 8, but in 7 of these the needle electrodes cou not be used In 1 case the muscles were definitely weak on the convex side

In 16 out of 19 idiopathic curves the muscles on the conve side were significantly stronger at the apex of the curv

Of 9 cases of congenital scoliosis the convex musc were stronger in 4, the concave muscles in 2, and the t sides equal in 3

In 8 cases (3 paralytic and 5 idiopathic) the muscle appeared equal or the concave muscles were stronge when superficial electrodes were used, but with needl electrodes the deep muscles were found to be considerabl stronger on the convex side In other cases, even thoug the convex muscles were slightly stronger with surface electrodes, the difference was far greater with needle electrodes (table II)

Interpretation of Results

In 16 of 19 idiopathic curves the muscles on the concave side were significantly weaker than normal We

TABLE IV—SUMMARY OF SALIENT FEATURES

Type of scoliosis	No of cases	Side of stronger muscles	No of cases in each category at each site			
			Needle electrodes at apex	Superficial electrodes at:		
				Apex	Abdominal	Intercostal
Thoracic paralytic	20	Ipse Contra Equal	7 0 1	12 0 8 *c*	5 *a* 8 6	7 *b* 3 9
Thoracic idiopathic	18	Ipse Contra Equal	9 0 3	10 0 8 *d*	3 2 13	10 2 6
ic congenital	11	Ipse Contra Equal	2 1 0	5 2 4	1 2 8	4 1 6
abar paralytic	8	Ipse Contra Equal	1 1 0	4 1 *e* 3 *f*	5 1 2	5 0 3
mbar idiopathic	1	Ipse Contra Equal	1 0 0	1 0 0	0 1 0	0 1 0
mbar spasmodic	1	Ipse Contra Equal	0 1 0	0 1 0	0 1 0	0 1 0

a In 1 case abdominal muscles not tested.
b In 1 case intercostal muscles not tested.
c In 3 of these, stronger muscles were "ipse" with needle electrodes.
d In 6 of these stronger muscles were "ipse" with needle electrodes.
e In this case needle electrodes were not used
f In 1 case stronger muscles were "ipse" with needle electrodes

gest that in some cases at any rate the most likely se for this is an unrecognised attack of poliomyelitis r findings support the theory that some cases of opathic scoliosis are really paralytic

If we now consider cases with much imbalance of the nal muscles—i.e. the known paralytic cases and the pathic cases, which are probably paralytic—we find at the weaker muscles are nearly always on the concave This is the opposite of what one would expect if deformity was caused by imbalance of the longitudinal muscles unopposed action of the longitudinal scles would tend to cause a curvature concave on the nger side

We suggest that in most of the cases we have examined, imbalance of the deep rotator and transverse muscles at is the main factor in producing deformity and that first stage in the genesis of scoliosis in such cases is rotation deformity due to unopposed action of the p spinal muscles. Our findings with needle electrodes firm this hypothesis

Summary and Conclusions

Muscle activity was investigated by electromyography 59 patients with scoliosis

In the overwhelming majority of these especially in alytic cases the spinal muscles were significantly nger on the convex side at the apex of the curve

Probably in nearly all paralytic and many idiopathic ses unopposed activity of the deep spinal muscles ses vertebral rotation and initiates the deformity

If muscle imbalance initiates the deformity it should possible to stop progression of the deformity by akening the stronger muscles A simple way of doing is to excise alternate laminæ and transverse processes the apex of the curve on the convex side

We wish to acknowledge with thanks the assistance of J Bryan McFarland, in whose department this work was and of the following surgeons who kindly sent patients investigation: Messrs H. G Almond H Osmond Clarke C Dwyer D Lloyd Griffiths, J R Hughes, K Marks O'Malley G V Osborne G T Partridge N W Roberts G K Rose

References at foot of next column

REDUCING OBSERVER ERROR IN A 70-MM CHEST-RADIOGRAPHY SERVICE FOR GENERAL PRACTITIONERS

PETER STRADLING
M.D Lond M.R C.P
CHEST PHYSICIAN

R N JOHNSTON
M.D Aberd., M R C.P
ASSISTANT CHEST PHYSICIAN

HAMMERSMITH CHEST CLINIC AND POSTGRADUATE MEDICAL SCHOOL OF LONDON

> *The roentgenogram is only as good as the person interpreting it, and therefore subject to the not inconsiderable limitations of human perception* (Garland 1949a)

THE necessity for dual reading of films to reduce observer error in chest radiography has been strongly emphasised in America and Denmark but as yet little in this country To the best of our knowledge no mass miniature radiography unit in the United Kingdom has adopted this procedure as a routine Indeed in a recent publication concerned chiefly with methods of increasing the efficiency of mass miniature-radiography services the Medical Research Council (1953) does not even mention dual reading

For the past two years it has been the practice in this clinic to offer to all local general practitioners a chest radiograph for any patient they feel requires this examination The responsibility of reporting a single film as normal without seeing the patient is great and it is very important to make the reading of these films as accurate as possible. In addition to under reading due to observer error small lesions may be missed in one of the blind areas of the standard postero-anterior film estimated to total some 25% of the lungs (National Tuberculosis Association 1950)

The problem was how to ensure accuracy without sacrificing simplicity and speed, which are essential in routine clinic work Our previous experience had suggested that the anteroposterior lordotic view might reveal lesions overlooked or concealed behind ribs or clavicles in a postero-anterior film and thus this view was used as a routine with the postero-anterior in an effort to reduce such errors which are inevitable if a single film is reviewed by one reader alone An added advantage of the routine use of two views is the ready elucidation of shadows due to clothing which occasionally cause confusion if seen on one film only

After the system had been in use for a trial period it seemed feasible to assess its value experimentally and to compare the diagnostic value of the additional film and that of an additional reader An experiment was therefore designed to investigate these points during the routine work of the clinic.

Method

For each patient standard postero anterior and antero posterior lordotic views were taken routinely on 70 mm film and read on the roll in groups of 50–100 at weekly sittings by two observers It was decided at the outset *to simplify the trial by excluding bony and cardiovascular* abnormalities from the investigation only shadows thought to represent conditions affecting the lungs pleura

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DR RIDDLE, MR. ROAF: REFERENCES

Bennett R. L. (1949) *Trans Int Poliomyelitis Conf* Philadelphia.
Clark J M P (1954) *Brit med J* ii 669
Colonna P C., Vom Saal F (1941) *J Bone Jt Surg* 23 335
Inman V T Saunders J B de C M. Abbott L. C (1944) *Ibid* 26 1
Jansen M. (1913) *Z Orthop Chir* 33 1
Loofbourrow G N (1948) *J Neurophysiol* 11 153
Lowman C. L. (1932) *J Bone Jt Surg* 14 63
Mayer L. (1936) *Ibid* 18 87
Steindler M. (1929) Diseases of the Spine and Thorax. St. Louis.

TABLE I—RESULTS DISTRIBUTED ACCORDING TO READERS AND VOTES FOR ACTION

	—	"No action" on both readings	"Action" on both readings	"No action" on postero anterior but "action" on combined reading	"Action" on postero anterior but "no action" on combined reading	Total
		Reader A				
Reader B	'No action' on both readings	I 440	II N = 30 A = 7	III N = 10 A = 0	IV 25	512
	'Action" on both readings	V N = 87 A = 15	VI N = 15 A = 160	VII N = 5 A = 2	VIII N = 8 A = 1	293
	"No action" on postero anterior but "action' on combined reading	IX N = 13 A = 1	X N = 3 A = 6	XI N = 0 A = 3	XII N = 1 A = 0	27
	Action' on postero anterior but no action' on combined reading	XIII 136	XIV N = 13 A = 3	XV 0	XVI 16	168
	Total	692	237	20	51	1000

and diaphragm were included The definitions of "normal" and "abnormal" would have presented some difficulty, so the problem was simplified by substituting "no action" and "action" Films had to be classified in one of these two groups by each reader on each reading, and it was found that the clinic routine was smoothly maintained by this classification, for it was the one used in practice when operating the X-ray service

To obtain independent assessments of the films each of the two readers (A and B) viewed them alone at separate sessions, recording his reports on the patients' record cards immediately This method abolished transcription errors since no secretary or written report intervened between the reading and the recording Furthermore, by using a punch card the subsequent analysis was facilitated

For the purpose of this trial two clip holes only were provided on the card for each reader the first for recording the report on the reading of the postero-anterior view alone before looking at the anteroposterior lordotic view, and the second for the combined report on the two films after seeing the anteroposterior lordotic view (this reading might confirm or refute the initial interpretation of the postero-anterior view alone) By not clipping or clipping each hole a report of "no action" or "action necessary" could be recorded on each reading, giving four possible combinations for each reader

(1) "No action" recorded for the postero anterior reading alone and for the combined report

(2) "Action necessary" recorded for the postero anterior reading alone and for the combined report

(3) "No action" recorded for the postero anterior reading alone but the combined report recorded as "*Action necessary*"

(4) "Action necessary" recorded for the postero anterior reading alone but combined report recorded as ' No action "

Only if either reader recorded "action necessary" on his combined report (postero anterior and anteroposterior lordotic), even if the other disagreed, was the patient recalled for appropriate large films The notations "N" and "A" ("normal" and "abnormal") were then applied to these cases to indicate the final agreed (or if necessary arbitrated) report on the further views Arbitration was necessary in very few cases, and the opinion of a senior radiologist was accepted

The interval (1 week) between the original small films and the subsequent large ones was sufficiently short to render negligible any errors due to change or disappearance of lesions in that time

A preliminary survey of about 200 cases revealed that at least 1000 would be required to reach any firm conclusions, and this number is here presented Records of a few more than 1000 cases were prepared, but 3 of the first 1000 had to be excluded subsequently because of failure to obtain large films The next consecutive 3 of the number over 1000 were then drawn on to produce the round figure to work with

Results

The findings on analysis of the 1000 cases are set out in table I, in which the squares are numbered consecutively with Roman numerals for ready reference A report of "no action" on all 4 readings was recorded fo 440, and these were accepted as "agreed normals' without further investigation (square I)

The other possibilities are displayed in the appropriat squares with the results of subsequent agreement (o arbitration) on large films indicated (N or A) By th addition of all those with the notation "A" a figur of 198 is obtained for the total "agreed abnormals' Percentages are related to this figure

By appropriate additions and subtractions of th figures presented in table I it is possible to assess th performance of the two readers and the value of addin readings or views to the reading of the standard poster anterior film The main significant findings are given i table II and show similar trends, varying in magnitud for the two readers For either, the lowest yield of th agreed abnormals is given by a single reading of th postero anterior films alone (89% and 91%) The figures can be increased to 98% when both readers mak a single independent report on the postero anterior fil alone The addition of a reading of the anteroposter lordotic view increased the abnormality yield for eac reader alone (to 91% and 94%) but not so effectively did dual readings of the single postero anterior film I fact dual reading of a single postero anterior film misse only 4 of the "agreed abnormals" (3 in square XI, in square IX) Furthermore on investigation these abnormalities proved to be minor shadows of doubtf significance The relative value of the methods in detec ing abnormals can be expressed graphically by usin the figures for the number of agreed abnormals misse by each procedure, and this is shown in fig 1

In assessing the true value of the various combinatio of readings the yield of abnormalities should be relate

TABLE II—COMPARISON OF RESULTS OBTAINED BY DIFFEREN READERS AND METHODS

Reader	Films read	No of agreed abnormals discovered	Agreed abnormals discovered as % of total agreed abnormals	Norma recall
A	Postero anterior alone	177	89	111
	Postero anterior and anteroposterior lordotic	181	91	76
B	Postero anterior alone	181	91	[illegible]
	Postero anterior and anteroposterior lordotic	188	94	13
Both	Postero anterior alone	194	98	34*
	Postero anterior and anteroposterior lordotic	198	100	[illegible]

patients called for further films who subsequently proved normal ("normal recalls") These are presented in the last column of table II It will be seen that single readings of the postero-anterior film gave high figures for normal recalls (particularly in the case of reader B) The addition of the second view however had a striking effect in reducing the number of normal recalls (from 111 to 76 for A, and 280 to 132 for B) The corresponding figures for dual reading show an equally striking saving when the anteroposterior lordotic view is added, and are presented graphically in fig 2 Had the lordotic view not been used in this trial an additional 157 patients would have been recalled This group has been termed "unnecessary recalls."

Discussion

The pioneer work in this field has come from America, where Yerushalmy and others (Yerushalmy 1947, Birkelo et al. 1947, Yerushalmy 1949, Garland 1949b Yerushalmy et al. 1950, Yerushalmy 1953) have reached the following broad conclusions:

(1) There is considerable subjective error in interpreting films (about 25% in these series)

(2) This can best be reduced by an independent second reader.

(3) Differences due to different types of film (e.g 35 mm and 14×17 in.) are negligible compared with the reader variation.

(4) The closest agreement between readers was obtained by ing descriptive reporting by a simple decision on "action" or "no action."

These conclusions are probably generally applicable Fletcher and Oldham (1949) Groth Petersen et al (19), and Cochrane and Garland (1952) have shown observer errors of similar magnitude Holm et al (1954) have re-emphasised the importance of independent dual reading

The Lancet (1954) while noting that previous work on this subject had often been under special test conditions suggests that under normal working conditions the consistency might be far greater It would be interesting to compare the results with those of an experiment made in the course of routine work and involving their routine decisions." Our results in routine practice confirm the tation of previous workers that independent dual reading reduces subjective error It will be seen that under reading when view single postero anterior films is 9–11%

In considering error which lower than that found by previous workers, factors may of some importance

(1) Whereas Yerushalmy's figures to minimal tuberculous lesions, our series contains the mixed abnormalities observed in routine practice— of them gross lesions.

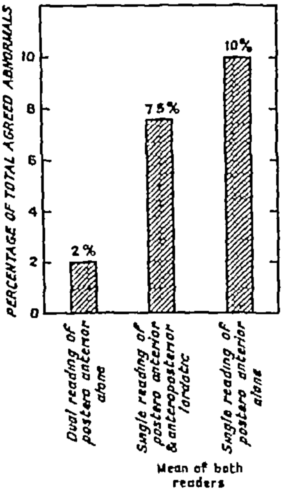

Fig 1—Agreed abnormals missed by various reading methods

(2) The agreed abnormals in Yerushalmy's papers are relatively small groups—61 of 1256 and 30 of 1790 We were fortunate to be dealing with a group containing a higher proportion of abnormals—108 of 1000

(3) The lack of an independent panel to define the "agreed abnormals" may have operated in our favour

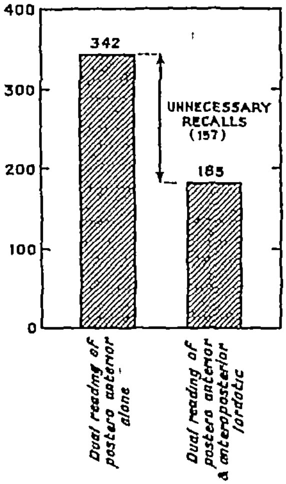

Fig 2—Normal recalls.

The anteroposterior lordotic film has certainly been of value in reducing observer error but more in avoiding "unnecessary recalls" than in increasing the abnormality pick up rate especially for reader B When it is remembered how much personal anxiety and loss of time these unnecessary recalls cause the anteroposterior lordotic view fully justifies the slight increase in staff time and expense In fact when 70 mm film is used double views, more expensive initially will ultimately reduce cost if patients recalled are radiographed on large film We consider that the result shown in fig 2 is as important as that in fig 1

Nearly nine years have elapsed since the presentation of the first paper on this problem and the chief conclusion —the importance of a second reading—is still neglected in this country It is probably natural to acknowledge blandly fallibility in others but not in oneself and this may explain reluctance to insist on dual reading We agree that an observer-error test is a "chastening experience" (Lancet 1954) and any who doubt this should themselves try the experiment

Objections to dual readings on the grounds of inadequate staff can surely be overcome Even when a second reader cannot be found a second independent reading by the same person can considerably reduce observer error (Yerushalmy et al 1950); it is hard to justify the continued practice of single reading of single films in routine chest radiography

Summary and Conclusions

In an effort to find a simple way of reducing observer error in a 70 mm chest radiography service single readings of one and two views were compared with dual readings of the same films

Two observers independently reading a single postero anterior film achieved greater accuracy than either alone

The addition of an anteroposterior lordotic view increased the abnormality yield of either reader working alone but was not so effective as the single view read by two observers.

Adding the lordotic view was of greatest value in avoiding unnecessary recalls

The best results were obtained by dual reading of the two views thus combining the advantages of both methods

Dual reading is essential in radiographic surveys and the routine use of the second view is of very great value in saving unnecessary anxiety time and expense

We sincerely thank Dr V H. Springett and Dr C M Fletcher for much help and advice during the trial and for constructive criticism of the manuscript, Dr R E Steiner for reading the films where arbitration was necessary, and Miss A. Keeble and Miss E Mangan for the radiography

REFERENCES

Birkelo, C C, Chamberlain, W E, Phelps, P S, Schools, P E, Zacks, D, Yerushalmy J (1947) *J Amer med Ass* 133, 359
Cochrane, A L, Garland, L H (1952) *Lancet* ii, 506
Fletcher, C M. Oldham, P D (1949) *Brit J industr Med* 6 168
Garland, L H (1949a) *Calif Med* 70, 29
— (1949b) *Radiology*, 52, 309
Groth Petersen, E, Løvgreen, A, Thillemann, J (1952) *Acta tuberc scand* 26, 13
Holm, S Nielsen, H, Møller, A V Winge, K (1954) *Ibid*, 30, 63
Lancet (1954) i 87
Medical Research Council (1953) Report of Sub-Committee on Mass Miniature Radiography M R C 53/687
National Tuberculosis Association (1950) Diagnostic Standards and Classification of Tuberculosis. New York, *p* 60
Yerushalmy, J (1947) *Publ Hlth Rep*, *Wash* 62, 1432
— (1949) *Calif Med* 70 26
— (1953) *Dis Chest*, 24, 133
— Harkness, J T, Cope, J H, Kennedy, B R (1950) *Amer Rev Tuberc* 61, 443

THE STERILISATION OF BLANKETS WITH CETYL TRIMETHYLAMINE BROMIDE*

ROBERT BLOWERS
M D Lond, Dip Bact
DIRECTOR

K R WALLACE
M B Camb, Dip Bact
ASSISTANT BACTERIOLOGIST

PUBLIC HEALTH LABORATORY (MEDICAL RESEARCH COUNCIL), MIDDLESBROUGH

It is well established that, in hospitals, blankets are an important reservoir of pathogenic organisms, and that freshly laundered blankets may be as heavily contaminated as those in use (Deicher 1927, van den Ende et al 1940, Thomas and van den Ende 1941, Rountree and Armytage 1946, Steingold et al 1954) The usual method of laundering blankets by a low-temperature wash does not sterilise them, and autoclaving is unsatisfactory because it produces gross shrinking and felting Oiling reduces the dissemination of particles from blankets, but there are objections to this process it is difficult to control, and the blankets may be unpleasantly oily, moreover, after some methods of oiling, organisms are still present

The use of quaternary ammonium compounds to sterilise blankets has been suggested by several workers

Rountree (1946) used an oil water emulsion stabilised with cetyl pyridinium bromide ('Fixanol C') Blankets treated with this emulsion were bactericidal for hæmolytic strepto cocci sprayed on to them from broth cultures Barnard (1952) also used fixanol C but did not oil the blankets Virtual sterility of both naturally and artificially contaminated blankets was obtained and some degree of residual bacteriostatic ability was noticeable

Steingold et al (1954) used tetra decylpyridinium bromide and alkyldimethylbenzylammonium chloride on naturally contaminated blankets and found very low bacterial counts after treatment

Vaughn et al (1948) rejected quaternary ammonium compounds because of their indefinite action in the presence of anionic synthetic detergents and soap

Objections to fixanol C are that it has an unpleasant odour, that it stains the blankets, and that it does not dissolve easily We therefore decided to try cetyl trimethylamine bromide, which is marketed as 'Cirrasol OD' (Imperial Chemical Industries Ltd) It is an odourless colourless cationic surface active agent which dissolves easily in water

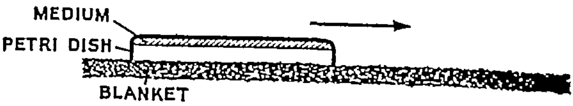

Fig 1—Method of sampling blankets.

Some of the previous work on the sterilisation of blankets is unrealistic in that artificially contaminated blankets were used and no attempt was made to neutralise residual disinfectant activity in the samples for culture In any experiment designed to test the bac properties of a chemical substance it is essential th samples taken for culture should be so treated that any of the disinfectant remaining in them (and possibly attached to viable bacteria) is neutralised If this is not done, the bacteriostatic properties of the substanc under test may prevent the growth of surviving organism and thus give rise to misleading results

We have worked entirely with blankets contaminate naturally while in use in hospital wards, and have incorporated in our culture medium a neutralising substanc for cetyl trimethylamine bromide

Materials and Methods

Cirrasol OD is an aqueous paste containing abou 12 5% of technical-quality cetyl trimethylamine bromid The consistence of the paste varies with the temperatur but the paste dissolves easily in warm water

Blankets were taken at random from those comm into a hospital laundry from medical and surgic wards

Sampling —The samples were taken by the swee plate technique This method was shown to us b Dr R E O Williams The blanket is laid flat on a tabl or may be sampled in its normal position on the be A petri dish containing a suitable culture medium, pressed upside down firmly against the blanket and swe across it fairly rapidly and evenly (fig 1) The moveme of the edge of the plate causes particles of dust an fluff to be thrown on to the surface of the medium Aft a little practice it is possible to adjust the pressure movement so that each plate is evenly spread with abo the same number of visible particles

The *culture medium* was nutrient agar containin 0 75% of 'Perminal COL'† It effectively neutralise any cirrasol OD which might remain active in the samp (fig 2) The colonies were counted after the plat had been incubated at 37°C for eighteen hours

Laundry Methods —The test blankets were washed i a Manlove and Alliot 34 × 54 in open pocket machin fitted with interrupter gear so that the inner contain is rotated intermittently This arrangement is bett than continuous rotation because it causes less felting an hardening of the blankets For a full load the machin was filled with water at a temperature of about 98°

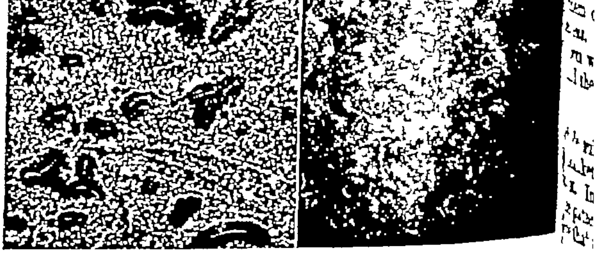
a *b*

Fig 2—Fibres from cirrasol-treated blanket causing: *a*, inhibition of *Staph aureus* on nutrient agar; *b*, no inhibition on perminal-agar

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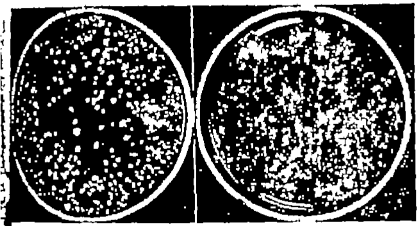
* This work forms part of an investigation by the Public Health Laboratory Service for the Newcastle Regional Hospital Board and is partly financed by a grant from the regional board

† Made by Imperial Chemical Industries Ltd, this is a mixture of non ionic surface active agent of the fatty alcohol/ethyle oxide type together with an anionic agent of the highly sulphate oil type


a b

1—Sweep-plates from blanket before (a) and after (b) treatment with cirrasol OD

7°C) to give a standing dip of 14 in Half a pint of Lissapol N'‡ and about 2 oz of soda ash (anhydrous dium carbonate) were added, and the machine was run for six minutes This was followed by one three minute rinse. The machine was next refilled with water at the same temperature as the wash to give a standing dip of 14 in., and 2½ pints of cirrasol OD was added to give a concentration of cetyl trimethylamine bromide of about 0 036% The blankets were left in this solution for minutes with occasional rotation They were next hydro-extracted and dried in warm air

The use of a non ionic detergent for washing is important. Soap and many other detergents are anionic and traces of them remaining in the blankets may inter with the action of the cationic cirrasol OD

ontrol blankets were treated by the routine method d in the laundry This involved washing with an ionic detergent followed by two rinses in water

Results

Treatment with cirrasol produced blankets from which ly occasional organisms were isolated (fig 3) The n colony-counts on 78 blankets before and after

TABLE I—SWEEP PLATE COUNTS ON 12 BLANKETS BEFORE AND AFTER TREATMENT WITH CIRRASOL OD

General bacterial counts on sweep-plates		General bacterial counts on sweep-plates	
Before treatment	After treatment	Before treatment	After treatment
2080	1	389	0
2300	10	313	7
1800	3	328	1
900	11	205	0
411	1	251	0
310	1	240	[illegible]

tment were 104 and 2 6 respectively In contrast routine washing procedure was much less effective mean counts for 42 blankets before and after washing re 340 and 208 respectively Tables I and II show the nts on the 12 most heavily contaminated blankets m each series.

After treatment with cirrasol the blankets were of mal appearance and texture and odourless. We were ble to show that cirrasol remained in the blankets by laing them over culture plates sown with *Staphylococcus aureus* After incubation the growth of the phylococci was completely inhibited in well marked s round the pieces of blanket fibre (fig 2a)

Discussion

The whole subject of the washing and sterilisation of hospital blankets deserves more thought than is often given to it. In many hospitals blankets are washed only if the patient dies or has had an infectious disease We believe that this is not only wrong but also dangerous. Many workers have now shown that patients in hospital quickly become nose and skin carriers of antibiotic resistant staphylococci Blankets are largely responsible for the transfer of these organisms from patient to patient, and should be washed and sterilised afresh for each new occupant of the bed Possibly this routine would be more acceptable to hospital authorities if the great damage done to blankets by heat sterilisation could be avoided.

The efficacy of quaternary ammonium compounds for the sterilisation of blankets has been suggested by the results of other workers who did not, however, neutralise residual disinfectant remaining in the blankets Their results have thus failed to show that organisms in the blankets are killed. The experiments reported here show that susceptible organisms are actually killed and not merely inhibited on the culture plates Sterilisation of blankets with cirrasol is simple and should be used as a routine procedure in hospital laundries The only precaution necessary is to ensure that preliminary washing is done with a non ionic detergent The first treatment of old blankets by the process we have described sometimes gives unsatisfactory results, but subsequent treatments achieve near-sterilisation We think that this is because the blankets contain a residue of soaps or of anionic detergents in which they were previously washed, which partly neutralises the bactericidal properties of cirrasol

TABLE II—SWEEP PLATE COUNTS ON 12 BLANKETS BEFORE AND AFTER WASHING WITH ANIONIC DETERGENT

General bacterial counts on sweep plates		General bacterial counts on sweep plates	
Before washing	After washing	Before washing	After washing
2000	740	800	190
7000	776	622	1028
2000	1332	600	600
1400	716	528	640
1028	260	379	75[illegible]
972	860	170	404

Cirrasol OD is less active against *Pseudomonas pyocyanea* than against many other organisms. It is, however, highly active against *Staph aureus* and this is of great value because of the increasing prevalence of infection of surgical wounds by antibiotic resistant staphylococci.

We have not yet been able to show to what extent cirrasol treated blankets retain disinfecting ability and hence influence the number of airborne organisms in the wards during bed making

The cost of the treatment above that of normal laundering is about 3½d a blanket The washing and sterilisation are however done as a continuous process, and separate handling of blankets, as in autoclaving is avoided The cost of the materials is therefore offset by a saving in labour

Summary

Blankets are an important reservoir of pathogenic organisms, because the routine low temperature wash does not sterilise them By a simple sweep plate technique large numbers of organisms were isolated from them

A method is described whereby blankets are treated with cetyl trimethylamine bromide applied in a laundry washing machine After this treatment only a few organisms were isolated

As distinct from similar previous work with quaternary ammonium compounds sampling was done on neutralising media to avoid misleading results from residual disinfectant in the samples for culture

We wish to thank Imperial Chemical Industries Ltd for providing materials and for technical advice Mr R I Aston for advice and assistance the laundry staffs at Poole Hospital Nunthorpe and at Crossgate Hospital Durham for their participation in the trials and Mr W R I Hollingsworth for some of the photographs

References overleaf

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‡ non ionic detergent manufactured by Imperial Chemical Industries Ltd.

ESTIMATION OF BLOOD-OXYGEN SATURATION

A NEW CUVETTE

C P HANDFORTH*
B Sc, M.B Lond
From the Department of Medicine, St Thomas's Hospital Medical School, London

Millikan (1942), Wood (1950), and others have described methods for the photo electric determination of the oxygen saturation of blood, but their apparatus is not generally available I describe here a simple optical cuvette for use in the Evan's portable photo electric colorimeter A preliminary report has been published (Handforth 1953)

Construction

The optical cuvette is constructed from 0 5 mm bore 'Polythene' tubing wound in a spiral over a 'Perspex' tube (fig 1), black silk is wound over the polythene spiral so as to lie between adjacent turns and occlude any light which has not passed through the lumen of the tubing The projecting ends of the perspex tube are painted black for the same reason The capacity of the cuvette is 0 2 ml and it may be used to analyse 0 5 ml samples

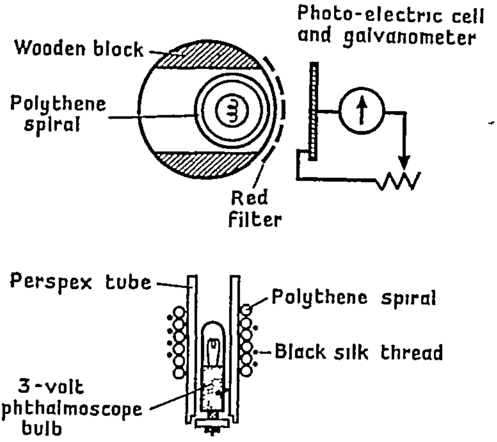

Fig 1—Diagram of apparatus The filter transmits only light above 600 Angstrom units and the photo-electric cell does not respond above 8000 A°

The source of light is an ophthalmoscope bulb placed inside the perspex tube, for zero adjustment of the galvanometer suitable resistances are placed in series with this bulb and in the photo electric-cell galvanometer circuit

The assembled cuvette and light source is mounted in a black perspex or wooden block with a window on one side covered with a red filter (Ilford 205 or Wratten 29), the block fits into the colorimeter

Calibration

The colorimeter has a logarithmic scale from zero to infinity The cuvette is filled with isotonic saline and the galvanometer set to infinity with the light off and to zero with the light on

To calibrate the oximeter a blood of known hæmoglobin content is serially diluted and the optical densities of fully oxygenated and fully reduced samples are measured (the blood is fully reduced with sodium hydrosulphite) Fig 2 shows the optical density curves for fully oxygenated and fully reduced blood plotted against the hæmoglobin values

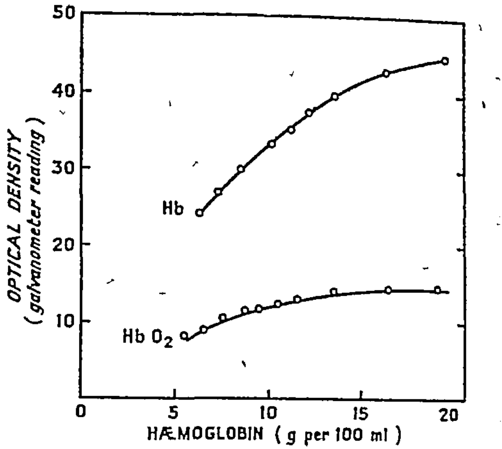

Fig 2—Optical-density curves for fully oxygenated and fully reduc blood of different hæmoglobin values.

It has been found that the difference in optical densit betw the fully reduced sample and the fully oxygenated sample blood is always the same for a given hæmoglobin value, fig 3 (uncorrected line) follows simply from fig 2

Method

For determining the percentage oxygen saturation any sample only two readings of the optical densi are needed (1) that of the sample on collection, and that of the sample after full oxygenation The opti density of a fully reduced sample is difficult to meas correctly, but it may be predicted from fig 2

Thus if a sample of blood is found to have an optical dens of 29 and the fully oxygenated sample an optical density 15, and the total hæmoglobin is 15 6 g per 100 ml., th the optical density of the fully reduced sample would 15 + 28 = 43 The percentage saturation would

$$\frac{43-29}{43-15} \times 100 = 50\%$$

In general terms $\frac{\text{reduced reading}-\text{test reading}}{\text{reduced reading}-\text{oxygenated reading}} \times$ = percentage saturation

The estimations are unaffected by the presence bile-pigments or plasma lipids, as these do not al the ratio of the optical density readings betwe reduced and oxygenated blood Errors in the hæm globin estimations have relatively little effect on calculated oxygen saturation because of the shall slope of the graph in fig 2 Moreover, it is usu unnecessary to repeat the fully reduced or fully saturat readings in a series of samples of the same blood Wh an absolute figure for oxygen content is required, estimation of the oxygen capacity is made by manometric method described by Van Slyke and N (1924)

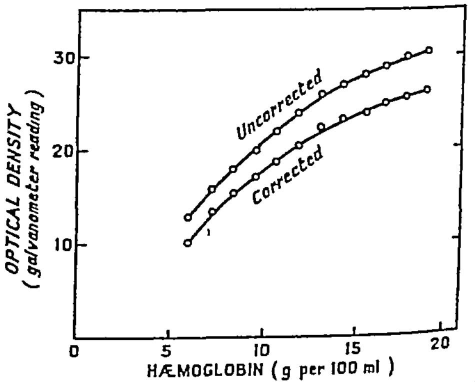

Fig 3—The difference in optical density between fully oxygenated and fully reduced blood for different hæmoglobin values.

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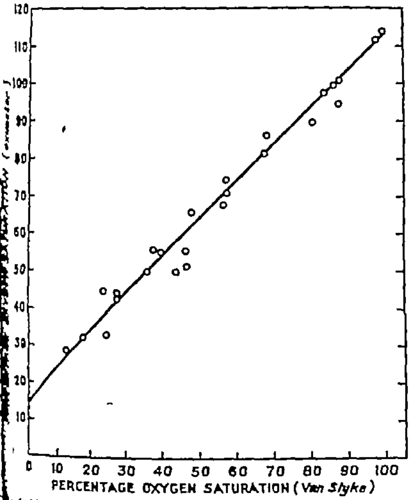
* Now at R.A.F Hospital, Changi, Singapore

DR BLOWERS, DR WALLACE REFERENCES

Barnard H F (1952) *Brit med J* i 21
Deicher H (1927) *Z Hyg InfectKr* 108 167
Rountree P M (1946) *Med J Aust* i 539
— Armytage J E (1946) *Ibid*, p 503
Steingold L Wood, J H F, Finch W E (1954) *J appl Bact* 17 159
Thomas J C van den Ende M (1941) *Brit med J* i 953
van den Ende M Lush D, Edward D G ff (1940) *Lancet* ii, 133
Vaughn T H Sotier A L Hill, E F Simpson J E Lee, W M (1948) *Industr Eng Chem* 40 2054



4—Linear relationship between percentage oxygen saturation as ermined with the oximeter and by the manometric method of n Slyke.

racy

When a series of estimations are carried out and pared with the results obtained with the mano ric method of Van Slyke and Neil (1924) the relation p is found to be linear (fig 4) but there is a systematic r which in the above example is + 14% at 0% ration This error depends on the quantity of ium hydrosulphite added to the samples in order to ain the readings recorded in fig 2 The values plotted the uncorrected line in fig 3 are therefore corrected reducing them by 14%

METER READINGS OF PERCENTAGE OXYGEN SATURATION ORRECTED VALUES) ON 25 SAMPLES, WITH THE RESULTS TAINED ON THE SAME SAMPLES BY THE MANOMETRIC ETHOD OF VAN SLYKE

Oximeter	Van Slyke	Oximeter	Van Slyke
38 1	44 5	88 5	87·0
76 0	81·0	81 0	83 5
71 6	84 5	72 5	60 0
31 5	24 5	18 5	16 0
13 6	13 0	30·0	26 0
61 9	68 0	5 0	49 5
31 0	57 0	12 5	38·0
47 0	58 0	87·0	88·0
35 5	47·0	86·0	86 5
11 5	10 0	37 0	36 0
29 0	28 0	68·0	68·0
100 0	100 0	19 0	25 5
[illegible] 0	98·0		

The accompanying table shows the results of 25 alyses fig 4 was constructed from the same readings t with the oximeter values corrected The standard riation of the method is ± 4%

Summary

A simple optical cuvette consisting of a spiral of thylene tubing is described for use in any photo ectric colorimeter for the oximetry of whole blood.

The method is reliable and rapid and requires only ml. blood

REFERENCES

Horth, C P (1953) J Physiol 120 43P
A (1947) Rev sci Instr 13 134
D D, Neil J M (1924) J biol Chem 61 523
H (1950) In Medical Physics Editor O Glasser
vol 2

IDIOPATHIC GRANULAR PROCTITIS

C F J Cropper
O.B E B.A. Oxfd F.R C P E.
PHYSICIAN BONKSWOOD HOSPITAL, WORCESTER

Published reports on idiopathic granular proctitis are surprisingly few and textbooks usually omit it from the differential diagnosis of rectal bleeding Price's (1947) index does not mention it

Brooke's (1954) description cannot be excelled:

> non specific procto sigmoiditis an insidious and indolent condition of the distal end of the large bowel has been observed by many but recorded by few A mild chronic and intractable inflammation is to be seen in the lowermost part of the rectum often limited to the last two or three inches with a sharply defined upper limit less frequently its distribution throughout the rectal ampulla is patchy On proctoscopy the rectal mucosa in the area involved is granular and bleeds to the touch Over the course of years the inflammation may spread upwards to involve the sigmoid and at this stage the sigmoidoscopic appearance is not dissimilar from that found in ulcerative colitis the onset is insidious and slow and there is no constitutional upset except when secondary anæmia results from constant blood loss.'

The condition is however distressing to the patient and a social handicap since the presence of blood in the rectum is apt to precipitate *diarrhœa*.

Sigmoidoscopic recognition is easy there is complete loss of the normal satiny sheen of the mucosa (Cropper 1945) whose place is taken by a coarse roughening of the surface due to the exposure of the deeper layers of the membrane.

The inflammation fluctuates unpredictably and no treatment can be regarded as specific

Since idiopathic granular proctitis has been so seldom described, I review here my own series of 26 cases (see table) This series excludes all cases of secondary granular proctitis, which fall into two groups those in which the granularity is a forerunner or concomitant of true ulcerative colitis; and those due to recurrent amœbic dysentery In both these groups the appearances are identical with those of idiopathic granular proctitis but in ulcerative colitis actual ulceration of the mucosa can often be seen with or without blood and pus flowing down from higher levels Such evidence of actual ulceration rules out by definition the diagnosis of idiopathic proctitis Similarly granulation occurring as a stage in recurrent amœbic dysentery must almost invariably be regarded as a sequel of acute amœbiasis. Evidence of its amœbic origin will be forthcoming from the history or from serial sigmoidoscopies at which scrapings from ulcers contain entamœbæ In many cases the metamorphosis over months of ulcers into pin point craters (Cropper 1945) and perhaps of craters into granularity eliminates benign proctitis from the diagnosis

Material and Findings

I have kept detailed records of about 2300 patients chiefly ex Servicemen involving about 2800 endoscopies between November 1946 and July 1954 11 of these presented with granular proctitis associated with ulcerative colitis 7 with granular proctitis following amœbic dysentery and 26 with the idiopathic granular proctitis Although 21 of these 26 patients had served in the tropics and most of them had been labelled dysentery' at some time in their service careful study of their history and repeated sigmoidoscopies and stool examinations provided convincing evidence of a non-dysenteric picture

This work was initiated when I was appointed to the then Ministry of Pensions Therefore most of the material

ANALYSIS OF CASES OF IDIOPATHIC GRANULAR PROCTITIS

Case no	Tropical service	Length of observation	Complications at sigmoidoscopy	No of sigmoidoscopies	Reply to final questionnaire	Original diagnosis
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2	No	1 yr	Nil	3	Asymptomatic	Granular proctitis
3	Yes	4 yr	Polyps	5 (1 almost normal)	Persistent blood	Amœbic dysentery
4	No	4½ yr	Nil	3 (1 normal)	Blood on and off, gaining weight	
5	Yes (P O W)	3½ yr	Nil	4 (1 normal)	Blood on and off, about 5 stools daily	
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7	Yes (P O W)	4½ yr	Polyps	4	Blood every few weeks	
8	Yes	4 yr	Nil	3	Periodic blood and diarrhœa	Amœbic dysentery
9	Yes	14 mos	Nil	2	No reply	
10	Yes	6 yr	Nil	3	Bouts of blood in spring	Clinical dysentery
11	Yes	6 yr	Nil	4	Diarrhœa and blood	Amœbic dysentery
12	Yes	5 yr	Nil	2 (1 normal)	Blood in attacks, weighs 14 st	
13	Yes	5½ yr	Nil	8 (2 normal)	Blood very occasionally, very fit	
14	No	4 yr	Nil	5	Blood now and again, no gain in weight	Dysentery
15	Yes	5 yr	Nil	5	Constant diarrhœa with blood and mucus, weight fluctuating	
16	No	1 yr	1 small polyp	4 (1 normal)	No reply	
17	Yes	4½ yr	1 polyp	2	Asymptomatic	Ulcerative colitis
18	Yes	4 yr	Nil	4 (1 normal)	Still passing blood general health good	Amœbic dysentery and bacillary dysentery
19	Yes	7 mos	Nil	3 (1 almost normal)	No reply	Amœbic dysentery and bacillary dysentery
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21	Yes, 1916 in Mesopotamia	3 yr	Nil	3 (1 normal)	Blood ceased 12 months ago, generally much better	Dysentery
22	Yes (P O W)	3 yr	Nil	2	Asymptomatic	
23	Yes	4½ yr	Nil	5	4 motions a day, no blood or mucus weight static	Amœboma
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The patients marked P O W in the table were in Japanese hands and therefore virtually deprived of diagnostic or therapeutic facilities for the first few years of their "dysentery" in these cases the past history of the disease was particularly obscure

The length of observation shown in the table is the period from when the patient was first seen by me until the date of the follow-up letter In 4 cases sigmoidoscopy was done at the end of the period of observation, which in all 4 cases was about four years

The follow-up letters show that in no case was the patient obliged to lose more than an occasional week's work thus even in cases with a six year history no gross deterioration has taken place In case 21 the disease has lasted more than thirty years without causing much inconvenience to the patient

Discussion

It is important that this syndrome should be clearly defined and kept in mind whenever rectal bleeding is under consideration If it can be diagnosed with precision, the patient can be assured that his disease is comparatively harmless, this is of great importance because rectal bleeding usually fills the patient with alarm and apprehension, and he is likely to torture himself with possibilities which he hardly dares to mention

There can be no doubt whatever that a very large number of patients with idiopathic granular proctitis were hastily and uncritically diagnosed as having some form of tropical dysentery and treated as such Indeed tracing back the history of such cases leads one into a tangle of vague diagnoses which in retrospect is impossible to unravel

The upshot of this is that, if the syndrome were widely recognised, the evacuation of personnel from forward areas would be minimised, and many an innocent victim would be saved from ill advised, expensive, unnecessary and often harmful therapy

I have often thought that the Forward Malaria Treatment Unit evolved in the late war might well be paralleled by a Forward Dysentery Treatment Unit, where the sigmoidoscope and the microscope could be used within sound of the guns Such a unit would be of incalculabl value in promoting immediate treatment of the tru dysenteries, and the immediate return to the front lin of patients with granular proctitis

Note on Treatment

It is my impression that phthalylsulphathiazol suppositories (Cluer 1947) have a place, albeit smal in controlling idiopathic granular proctitis It is tru that, since no infective agent has been incriminated, th use of an antibacterial drug is empyrical Plain coco butter suppositories are probably just as effective, an it is worth prescribing these, particularly in periods o quiescence Although severe secondary anæmia was no observed in this series it can develop (B N Brooke personal communication) and would indicate iro therapy Probably the most valuable part of thi treatment is reassurance

Summary

26 cases of idiopathic granular proctitis are reviewed

The recognition of this syndrome is important, so that it can be clearly distinguished from the more serious conditions of which it may be a forerunner, a concomitant or a sequel

I wish to thank Mr B N Brooke for his advice during the preparation of this article Seeing that war pensioners medical documents have been used, it is fitting that acknowledgment should be made to the Ministry of Pensions and National Insurance for permission to use these records.

REFERENCES

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Cropper, C F J (1945) *Ibid* ii, 460
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Reviews of Books

Diagnosis and Treatment of the Acute Phase of Poliomyelitis

And its Complications Editor: ALBERT G BOWER, M.D Baltimore: Williams & Wilkins London Baillière Tindall, & Cox. 1955 Pp 250 50s

THIS authoritative and timely statement of American practice comes from the Los Angeles County Hospital—second largest communicable-disease hospital in the United States—and it is based on an experience of over 15,000 cases, 11,000 of them in the last seven years The main clinical problems are dealt with in turn by the editor and other physicians, by the nurse, otolaryngologist, radiologist, physical medicine specialist, obstetrician, biochemist, and other experts. The team is united in its *advocacy of early elective tracheotomy* combined with use of the tank respirator for bulbar poliomyelitis with respiratory involvement. Although no statistical evaluation is attempted (except on a small scale in a final chapter by a county medical team which adopted the same methods), the pros and cons of the team's technique seem to have long passed the stage of academic discussion and we are clearly dealing with a fait-accompli.

Technical *requirements are naturally far from simple* the special equipment required by a unit includes a Bennet respiratory ventilation meter for accurate measurement of tidal air and vital capacity a positive-pressure attachment exactly synchronised with the cycle of the respirator a humidifier attachment, an intermittent positive pressure breathing unit of the demand flow type and a juvenile respirator *First-class laboratory facilities for control of* blood chemistry are also required. Finally the well integrated team of medical and surgical specialists and of experienced nurses must be ready for action at any moment Under such conditions results got progressively better Some 60–80% of respirator patients had tracheotomies.

The book is excellently produced and the illustrations are well chosen. Clinicians dealing with acute poliomyelitis will find it stimulating and helpful.

Medical History of the Second World War

The Army Medical Services Administration. Vol. II Editor: F A E CREW F.R.S H.M. Stationery Office 1955 Pp 504 65s

THE subjects of this volume are preventive medicine in its military aspects and other activities of the medical services outside or ancillary to the collection and treatment of the sick and wounded. Nursing dentistry, pathology radiology blood transfusion, psychiatry and ophthalmology—each has a chapter tracing its growth during the war and the *changes in its organisation* to meet the needs of the hour Strictly medical and technical commentaries will appear in later volumes. Administrative detail is likely to make dull reading but those with long memories will find some persuasive explanations of incidents which seemed addle-pated muddling at the time.

Of greater interest and importance are the chapters on "hygiene"—a word which in the Army embraces an empire which must be the envy of the most ambitious nation It came as a shock to some civilians in khaki to find that while they seemed to be more knowledgeable at the bedside (perhaps they had had more practice) the boot was on the other foot when they met the problems of keeping the *Army fit to fight. The Army School of* Hygiene has yet to receive its due of praise for solid research and ingenious innovation War brought to it new problems and this account ranges over the ration scale the design of uniforms, medical categorisation (which might have been expanded) environmental hygiene and the health of those who fought in tanks It really deserves a volume to itself

There are other reasons for reading this book than one which to recapture a taste of the purposeful energy of ten years ago. It is a monument to many anonymous men whose efforts brought victory from near-defeat It includes many hints and suggestions which deserve further inquiry in these quieter days

Operative Orthopedic Clinics

LEWIS COZEN M D F.A C.S assistant professor of orthopedic surgery College of Medical Evangelists, Los Angeles; ALVIA BROCKWAY M.D chief of staff Orthopedic Hospital, Los Angeles; in collaboration with PAUL E MCMASTER, M.D F.A.C.S., clinical professor of orthopedic surgery University of California Philadelphia J B Lippincott London: Pitman Medical Publishing Company 1955 Pp 329 80s

IN their preface the authors say: "An attempt has been made figuratively *to allow the reader to take* his place in the operating room of two busy orthopedic services. After the dictated report, the reader will find some remarks similar to the verbal comment the surgeon might make during and after the actual surgery" And later 'Had the operative reports been dictated more carefully, a more lucid picture of the operation would be *present in many instances* They do not pretend to cover all orthopædic operations, and their choice appears rather haphazard On the whole the *descriptions of* procedures are clear enough, though—with the method they use—there is necessarily much repetition. The main interest however lies in the subsequent comments, which cover a wide field not always directly relevant to the operation under discussion Though it is extremely hard for the reader to get a balanced view of the indications for any *particular procedure he will pick* up many valuable tips on overcoming the difficulties that can arise during operation

The book is largely an account of individual technique, and this of course may differ widely from our own. But it is not easy to believe that displacement of the patella is ever necessary for the removal of an external meniscus or that removal of one-third of the proximal phalanx is sufficient in Keller's operation The illustrations leave *much to be desired, some* being pointless, and others positively misleading Technique can be better learnt, on the whole, from the standard textbooks *on orthopædic* operations but the surgeon with some experience behind him will find much to interest him.

Experimental Psychology

Revised edition. ROBERT S WOODWORTH Columbia University HAROLD SCHLOSBERG Brown University London: *Methuen. 1954 Pp 948 £3 3s*

IN the course of his long life—he was born in 1869—Professor Woodworth has rendered great services to psychology as investigator and teacher; among the most valued of his *contributions has been his* handbook of experimental psychology The historian of this subject, E G Boring said of Woodworth that he "came as near to being the general experimental psychologist as any important man ever did," and the range of his activities and experience justifies this extreme statement. Allied with his exceptional gift for lucid exposition it enabled him to bring out a book *of remarkably* catholic completeness within its declared scope. The first edition appeared in 1938 after eight years of determined work in preparing it. In 1940 Professor Woodworth and his collaborator undertook the present thoroughgoing revision. *The book contains* more material than before but is not bulkier Historical surveys have been greatly reduced and some chapters (e g *on feeling and* experimental æsthetics) have been dropped The magnitude of the authors' task may be gauged from the size of the bibliography—about 2480 titles half of which had not been used for the first edition. The chapters on emotion and *on learning have been* reorganised in accordance with current development in these fields.

This *is not a handbook* of psychology It largely omits for example the field of individual differences, social psychology, much of animal psychology, child development and applied psychology the name of Freud does not appear in the bibliography nor Piaget nor MacDougall It is concerned only with experimental psychology which is not the whole of psychology but the most solid and *communicable* part and that which experimental biologists generally and physiologists in particular will find closest to their own scientific *problems* and habits of thought It is in its own field a masterly standard work.

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Virus and Rickettsial Diseases

2nd ed S P BEDSON, M.D, D SC, F R C P, F.R S, A W DOWNIE, D SC, M.D, F R S, F O MACCALLUM, B SC, M D, C H STUART HARRIS, M.D, F.R C.P London Edward Arnold 1955 Pp 407 30*s*

IT is no surprise that a second edition of this commendable work has been called for after five years Knowledge of viruses has increased so rapidly that there is much to be added or modified. Reviewing the first edition, we suggested that more would soon be needed about poliomyelitis following inoculations and about the Coxsackie viruses and the expected additions have been made, the Coxsackie viruses now having a chapter to themselves Naturally there is also a discussion about poliomyelitis vaccines, and it is very apposite There is a new section on virus multiplication, but the chapter on bacteriophages has been dropped Altogether the book is as up to date as could be hoped for there are references to cultivation of varicella and the viruses of acute respiratory disease, though not to Enders's recent work on measles

Weltraumstrahlung

Der heutige Stand der biologischen Erforschung J EUGSTER, Privat-Dozent, University of Zürich Berne and Stuttgart Hans Huber 1955 Pp 141 Sw Fr 26 00

THIS is an up-to-date review of the present state of knowledge of cosmic radiation, by an author who has made considerable contributions in this field

The book is divided into two main sections, the first being devoted to the physical properties of cosmic rays, and dealing in turn with heavy primary particles, star producing nucleon components, neutron components, electron showers, and the relative intensities of the components at various locations above and below the surface of the earth The emphasis is on the possible biological effects of the physical phenomena discussed

The second main section deals with methods of investigating the biological effects of cosmic rays Three methods enabling the investigator to determine which cells have been the targets of cosmic ray components are reviewed The first consists of placing a regular pattern of test objects in close proximity to two layers of nuclear emulsion, the second involves the injection of emulsion directly into the tissues under investigation, while the third relies on the photochemical action of incident radiation on certain dyes (e g, triphenyltetrazolium chloride) or enzymes (e g, ATPase) In a critical discussion of the results obtained by these methods, Dr Eugster emphasises particularly the importance of examining the effect of cosmic rays on individual cells rather than on whole tissues or animals

Two of many questions still requiring answers are whether exposure to heavy primary particles and to nuclear disintegrations can convert precancerous to malignant cells and whether induction or growth of spontaneous or chemically induced tumours may be influenced by maintenance in an environment of low radiation level There are more than 400 references.

Textbook of Gynæcology (4th ed London Heinemann Medical Books 1955 Pp 490 27*s* 6*d*)—Gynæcology, Mr J H Peel implies in the preface to his fourth edition, has stood reasonably still for the past five years—anyhow as far as medical students need be concerned. This has left him free to revise his text without major rearrangement, to include new theories about disorders of menstrual function, and to exclude syphilis, which is now so come down in the world as to claim no place in a textbook of gynæcology Dr E W H Shawcross has rewritten the section on X ray treatment, and a new set of drawings of the principal gynæcological operations, by Mr R N Lane, will be welcome to students

The Diabetic Life (15th ed London J & A Churchill. 1955 Pp 228 12*s* 6*d*)—Dr R D Lawrence's book has been a practical guide to the treatment of diabetes for thirty years. This edition includes advice on the use of the new insulins, and other fresh matter

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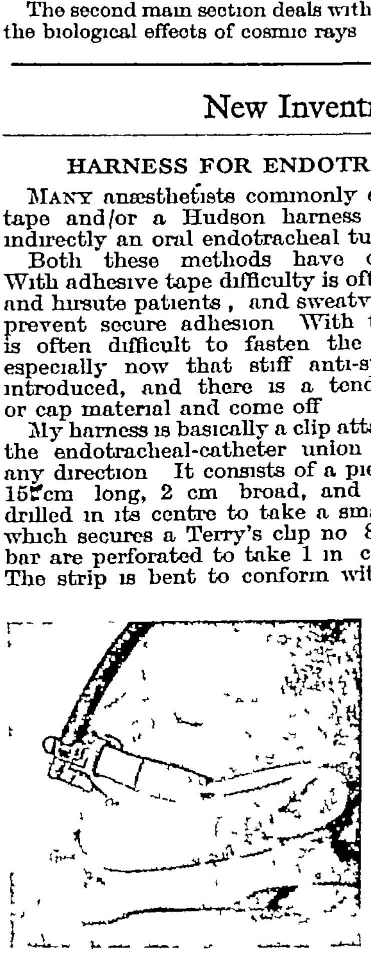
New Inventions

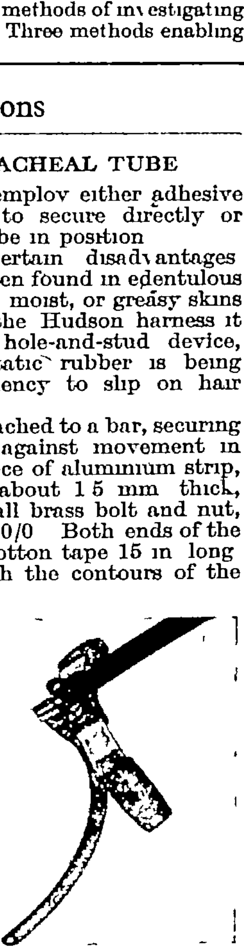
HARNESS FOR ENDOTRACHEAL TUBE

MANY anæsthetists commonly employ either adhesive tape and/or a Hudson harness to secure directly or indirectly an oral endotracheal tube in position

Both these methods have certain disadvantages With adhesive tape difficulty is often found in edentulous and hirsute patients, and sweaty, moist, or greasy skins prevent secure adhesion With the Hudson harness it is often difficult to fasten the hole-and-stud device, especially now that stiff anti-static rubber is being introduced, and there is a tendency to slip on hair or cap material and come off

My harness is basically a clip attached to a bar, securing the endotracheal-catheter union against movement in any direction It consists of a piece of aluminium strip, 15 cm long, 2 cm broad, and about 1 5 mm thick, drilled in its centre to take a small brass bolt and nut, which secures a Terry's clip no 80/0 Both ends of the bar are perforated to take 1 in cotton tape 15 in long The strip is bent to conform with the contours of the maxilla at the level of the upper lip The bar is padded at either end with rubber guards 4 5 cm long covering the junction of the bar with the cotton tape The bolt head in the middle of the bar is padded on the facial side by 2 cm of 5 mm. thick sponge rubber secured by rubber bands 1 cm wide at either end The jaws of the Terry's clip are covered by 1 cm of anti static rubber on each





After the introduction of an oral cuffed or uncuffed tube the clip is placed in position beneath the nose, and the endotracheal-catheter union is pushed into place between the jaws of the clip The rubber-tubing connection to the anæsthetic-gas supply is then attached without any further securing device One tape is passed behind the neck to tie with the other at the side of the jaw In practice this gives absolute security against all untoward sudden movements often experienced in moving the patient into position in the theatre, and in giving controlled respiration It is in such manœuvres that small movements of the endotracheal tube can give rise to troublesome "bucking" in a lightly anæsthetised patient

The harness has been designed with the Waters to-and fro apparatus in mind but can be used with the usual heavy corrugated connecting tubing This size clip (80/0) will hold Rowbotham's union piece, Magill's nasal, oral, and suction T-pieces, Gillespie's, Cobb's suction union, and Ayres T-piece Nosworthy's middle-size endotracheal unions are also taken, but the larger and more angular unions of this type are less securely held

This clip has been used for securing oral endotracheal tubes in more than 100 patients aged 2–75 years, and requires no bending or manipulation once it has been moulded to the contours of the average maxilla It will also withstand repeated boiling and, provided that the rubber tubing delivering the anæsthetic gases is anti static, does not require further earthing

The harness is obtainable from Medical & Industrial Equipment Ltd, London.

County Hospital,
Huntingdon

HEDLEY ROLFE
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THE LANCET

LONDON　SATURDAY JUNE 18 1955

By any Other Name

The beguiling euphemism "observer variability" has now been applied to the mistakes in interpreting radiographs It is quite clear that a single observer attempting to pick out cases of pulmonary tuberculosis from a largely normal population is likely to overlook about a quarter of the abnormal films This proportion has been remarkably constant in repeated trials in several countries, and any variation is more likely to be due to variation in the composition of the population (and especially to the number of difficult borderline cases) than to any difference in skill. Tests of observer error reveal, in addition to the frank "misses," a great lack of consistency An observer is likely to disagree with his colleagues concerning one in five of the positive cases, though he is a little more consistent with himself, when given the opportunity—for instance, in assessing progress—he swings from 'better' to 'worse" at second examination of a film in 7% of cases [1]

The reasons for this surprising state of affairs are not clear but failure to detect very slight changes is not the only factor, for it is not only the minimal cases that are missed Groth Petersen and Møller [2] have shown that of the cases missed on a single reading 86% were sputum positive, 35% were of bilateral disease and in 15% there were cavities. Nor are the "misses" necessarily lesions difficult to spot given a second chance, the observer may immediately detect the abnormality and be amazed that he ever overlooked it It also seems unlikely that the speed of working is an important factor for though test material is sometimes examined rather hurriedly abnormality is usually quickly spotted and prolonged searching does not yield many more cases—though it rapidly increases fatigue Perhaps boredom and the hypnotic effect of the repeated normal are more important Opinion can easily become biased in favour of the predominant, after reading many more or less orm films the observer becomes less inclined to ark on the slightly exceptional Accuracy might ease if test films were read in small batches of twenty to twenty five once or twice a day, an eriment on these lines would be valuable It has n suggested [3] that the conditions of the tests are ly responsible for some of the inaccuracies and onsistencies they reveal the observer has a sense of m and is forced to reach decisions not made in tine practice. Thus the tests probably present the ture at its very blackest Nevertheless attempts test observers without their knowing it have not supported the soothing notion that the observer is much less fallible in ordinary routine work.

One of the more surprising conclusions from these tests is that small films, properly used, can be as reliable for the detection of tuberculosis as the conventional full sized films—but only if they are interpreted independently by two readers Fortunately small films are easy to handle and can be readily viewed in special illuminators or projectors in batches of 50–100 A year ago [3] we suggested that the simplest and most effective way of increasing the efficacy of chest radiography surveys would be by dual reading This contention is supported by Clayson et al, [4] and by Dr Stradling and Dr Johnston whose article appears on an earlier page of this issue Clayson et al set out to determine whether 70 mm. photofluorography is a safe and proper method for chest-clinic work By an ingenious and thorough analysis of their results much more was brought to light They found, firstly, that for the detection of tuberculosis independent dual reading of 70 mm film can be as effective as single reading of large films Secondly, they found that accuracy and consistency improved when simple classifications were used, and were greatest when only "clinically significant" cases were being sought (An attempt to determine which films showed "active lesions" produced the greatest variability underlining the absurdity of trying to do this by radiography alone) Thirdly, they determined the most reliable method of case-finding Results were best when the small films were used solely to select cases needing further investigation. When the films had been read independently by two readers, all the cases questioned by each reader were recalled The large films then taken were also read by both readers independently Even under these rather exacting conditions the cases of active disease that were missed and were subsequently detected amounted to an additional 20% or so

Stradling and Johnston report their experience with 70-mm film at the Hammersmith Chest Clinic Well aware of the dangers of single observations, they make independent dual reading the rule, and they confirm the increased yield of cases This double-checking inevitably increases considerably the number of patients recalled for further investigation most of whom will prove to be free from disease In an attempt to avoid some of the fruitless increase, they took, in every case, two films—an ordinary postero anterior projection and an anteroposterior lordotic projection. The results seem very satisfactory the number of recalls dropped from 111 to 76 for one reader from 280 to 132 for the other, and from 342 to 185 for both together This is a most important observation. Small films can compete in accuracy with large films only if dual reading is adopted, but the consequent increase in recall rate (which is sometimes almost doubled) has been regarded by many as an overwhelming objection to this method —particularly when applied to industrial workers at the factory or pit during working hours when the temporary withdrawal of a single person may put a whole team out of action. But is dual reading of two films in every case more trouble than it is worth? Would it be more economical, easier, and safer to use

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Yerushalmy J., Garland L H, Harkness J T, Hinshaw H C, Miller E R, Shipman, S J., Zwerling H B *Amer Rev Tuberc* 1951 64, 225

Groth Petersen E., Møller A. V Cited by Clayson et al. (footnote 4).

Lancet, 1954, i 67

[4] Clayson C, Frew H W O, McIntosh D G, McWhirter J G, McKinlay I I., Stein, L *Brit J Tuberc* 1955 49 51

large films from the start? The real advantage of miniature photofluorography is that it can deal with very large numbers, but for the examination of smaller numbers its advantages are less obvious Certainly those particularly exposed to risk of infection—such as tuberculosis contacts, nurses, or medical students—should not be given clean bills of health on the single reading of a miniature film, and there is much to be said for using large films—read twice—to examine such smaller groups, who for one reason or another are already preselected So far photofluorography has been found reliable only for the detection of tuberculosis, and this method is not necessarily equally valid for detecting shadows of a different quality—for instance, those of pneumoconiosis[5] In the early stages of a dust disease the lesions are smaller and softer, and are best seen towards the periphery of the lungs, where in miniature films the definition may be impaired by spherical aberration. The suitability of small films for this purpose can be proved only by experiment, but this would be no simple matter, since numbers would have to be large and the investigation most carefully planned to make full allowance for the effect of observer error

Whatever the purpose of the examination, and whatever the size of the film, it is now apparent that the radiograph should preferably be read by two observers

Biochemical Disturbance in Hepatic Coma

THE association of mental disturbance with hepatic disease has been recognised since the days of GALEN, but even now the underlying mechanism is far from clear The term "cholæmia," introduced by LEYDEN[6] in 1866, by analogy with uræmia, implies that the essential fault is in excretion This hypothesis has had to be abandoned owing to the absence of "cholæmia" in cases of complete biliary obstruction and the failure to incriminate any of the known constituents of the bile The known functions of the liver now amount to several hundred (and doubtless many more remain to be discovered), so it is hardly surprising that the disturbances responsible for the cerebral disorder have not been easily elucidated All recent work suggests that the cause is either a breakdown in the detoxicating function of the liver or liberation of a toxic by-product of its disordered metabolism

In view of the essential rôle of the liver in carbohydrate metabolism, and the death in hypoglycæmia of laboratory animals after hepatectomy, hypoglycæmia might reasonably be expected to be a conspicuous feature of hepatic failure Yet with few exceptions the blood-sugar levels of patients in hepatic coma are within the normal range Disturbances of blood electrolytes resulting from the hepatic disorder and the massive intravenous glucose injections with which it is often treated are a largely avoidable, but relatively uncommon, cause of cerebral symptoms WALSHE'S[7] study of the amino-acids in the blood, urine, and cerebrospinal fluid of patients in coma and precoma revealed more consistent abnormalities, of which a rise in the level of glutamine, and sometimes also of glutamic acid, was the most striking

On the basis of these findings WALSHE "suggeste tentatively that changes in the amino acid pattern of the body fluids are capable of producing varyin neurological syndromes," including hepatic coma A few years earlier it had been found that administra tion of ammonium chloride to patients with cirrhosi sometimes induced neurological complications[8], an it seemed that the raised glutamine level found b WALSHE in the cerebrospinal fluid might resul from a detoxication mechanism by which the highl toxic ammonium radicle was removed—namel by combination with glutamic acid to form the amid glutamine According to this view, cerebral symptom associated with hepatic disease are the result o ammonia intoxication The recent findings o Dr SHERLOCK and her associates[9] confirm th correlation between the blood-ammonium level and the appearance of cerebral symptoms These workers point out that such a rise can result either from failure of the injured liver to deal with the ammonia arriving via the portal vein or from by-passing of the liver by the collateral circulation provided by portal-systemic anastomoses They emphasise that since neurological changes can occur without a significantly raised blood-ammonium level, and identical changes can be precipitated by orally administered methionine, the relation of blood-ammonium level to hepati coma may be similar to that of the blood urea level to uræmia—i e, a correlation exists but it is not causal This hypothesis attributing the cerebral symptoms to ammonia intoxication has led to the use of large doses of glutamic acid in the treatment of hepatic coma[10] In a small number of patients with hepatic cirrhosis the response to this treatment was quite dramatic But the results are inconsistent and unpredictable, and in patients with massive necros they have been uniformly disappointing Dr WALSHE in a paper published this week on p 1235, confirm these experiences He emphasises that the stat of the intracellular mechanism dealing with exces ammonia is more important than the ammonium level in the blood Thus cerebral disturbance could arise from an intracellular defect of this mechanism in the presence of a normal blood-ammonium level and conversely levels usually regarded as toxi could be tolerated in the presence of enhanced intra cellular detoxication BESSMAN and BESSMAN[11] have shown, by a study of the arteriovenous differenc of blood-ammonium, that there is a considerabl peripheral utilisation of ammonia, presumably in muscle Levels of ammonia in systemic venous blood may therefore give no reliable indication of the level in the arterial blood reaching the brain, and this could account for some of the discrepancies recorded by SHERLOCK BESSMAN and BESSMAN have also shown that in the presence of a raised blood ammonium level there is considerable intracerebral utilisation of ammonia with a corresponding increase in the cerebral arteriovenous difference Such utilisation might be due to synthesis of glutamine, but this requires adenosine triphosphate and would result in an enhanced oxygen uptake, whereas the available evidence shows that in coma and precoma uptake of oxygen by the brain is depressed. BESSMAN and BRADLEY therefore suggest that the main reaction consuming ammonia is the conversion by reductive amination of α ketoglutaric acid to glutamic acid. This could result in the removal of α ketoglutarate, an essential member of the Krebs cycle, and consequent reduction of the oxidative metabolism of all those metabolites with which this cycle normally deals—a disturbance that would explain the rise in blood pyruvate and glutamate.

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[5] McCallum R I Browne R C *Brit J industr Med* 1952, 9 99
[6] Leyden E Beitrag zur Pathologie des Icterus Berlin, 1866
[7] Walshe, J M. *Quart J Med* 1951, 20, 421
[8] Phillips, G B Schwartz R., Gabuzda, G J jun Davidson, C S *New Engl J Med* 1952, 247 239
[9] Phear, E Sherlock, S Summerskill W H J *Lancet*, April 23, 1955 p 836
[10] Walshe J M *Ibid* 1953, i, 1075
[11] Bessman, S P Bessman, A N *J clin Invest* 1955, 34 622

The metabolic activities of the liver are so complex that the mental disturbances in patients with hepatic disease would hardly be expected to depend always on the same biochemical disorder. The presence of "fœtor hepaticus" in patients gravely ill with disease of the liver directs attention to toxic metabolites other than ammonia. Professor CHALLENGER and Dr WALSHE report (also in this issue) the isolation from the urine of such a patient of methyl mercaptan and dimethyl disulphide. These products are derived from methionine by chemical reactions known to occur in vivo. The greatly increased blood level of methionine in hepatic disease—probably the result of impaired capacity of the injured liver to handle this amino acid—presumably favours the abnormal metabolic pathway that leads to these odoriferous sulphur compounds. That they are toxic seems likely. Other possible products of disordered methionine metabolism arising from partial oxidation, such as the sulphoxide and the sulphone, may contribute to the clinical picture.

Recent work on the mechanism of hepatic coma thus incriminates ammonia and various sulphur-containing by-products of disordered methionine metabolism. That these comprise by no means all the complex biochemical machinery that relates hepatic to cerebral dysfunction is almost certain. Since there is probably no single cause of hepatic coma would it not, as WALSHE suggests, be advisable to refer to "the hepatic comas"?

An Incomplete Reform

UNWITTINGLY King GEORGE III did much to take the stigma of moral guilt from insanity. The effects on public opinion and on lunacy reform of his first attack of mental illness were (Dr KATHLEEN JONES writes[1]) intangible but real. On his recovery in 1789

the people were warmly sympathetic; there was for him none of the condemnation then usually accorded to the insane.

> "Nobody suggested that the King was being punished by heaven for his sins; nobody regarded him as being possessed by the Devil; insanity had become a respectable malady—one which might happen to anybody; and, which is even more important, one which was susceptible to treatment and capable of cure."

Not that the treatment accorded to the King was in any way more enlightened than that suffered by other mental patients at the time; he was purged, beaten, starved, and kept in bonds like the rest. But his illness marked a turning point; for, though there had already been some stirrings of concern about the fate of the insane, little had been achieved before that time.

In the early part of the 18th century the medieval conception of charity as a duty every man owed to his neighbour was dying out, and there was no corporate sense of responsibility to take its place. The insane were not regarded as any kind of separate group; if mental illness brought them to penury they came under the poor law; if it caused them to commit a crime they were judged under the penal code; if they wandered without means of support they came under the vagrancy laws. Bethlem was the only institution of public standing which dealt with the mentally abnormal; and Bethlem—"Bedlam"—was passing through its terrible years. The rich might be kept at home or sent to small evilly run madhouses which offered a pledge of absolute secrecy; the poor were kept in such holes and dark corners as their family chose, or sent to a workhouse or prison. Many still fell under suspicion of witchcraft; and, though the penal laws against witchcraft were repealed in 1736, there were still plenty of people in far villages to try by ordeal insane people suspected of dealings with the devil. Standards of professional training in medicine were miserably low, and treatment was directed to weakening the insane patient by the systematic use of purges and emetics, by bloodletting, blistering, and cautery. The clergy held that human misery was the result of personal sin, while philosophers believed in "natural law" and took the world as they found it, lunatics and all. Pauperism from other causes than insanity was increasing; and the name "workhouse" carried with it, as an official publication of 1732 noted, "an idea of Correction and Punishment." In 1789, when GEORGE III journeyed to Weymouth for his convalescence, there were in workhouses—where punishments for not working or for "mischievous conduct" included solitary confinement in a dark room and deprivation of food—some 4000–5000 psychotic or mentally defective people. Many others were in prisons or bridewells.

Yet as early as 1742 a select committee set up to revise the vagrancy laws had paused to consider dangerous lunatics; and the Act which resulted from their recommendations did at least order that the warrant of two or more justices of the peace should be required for their detention instead of only one justice as for any other vagrant. By 1763 some facts about conditions in private madhouses had become public, and had led to a movement to get statutory supervision of such places. A select committee was appointed; but a Bill to control the abuses was not introduced till ten years later, and then it was rejected by the Lords. An Act for Regulating Private Madhouses was indeed passed in 1774; but was so weak and ineffectual that it produced little change in the contemporary scene. Nevertheless, Dr JONES points out, it did establish five important principles: that private institutions run for profit should be licensed by a public authority; that the reception into them of people alleged to be insane should be notified; that commissioners whose method of appointment should be prescribed by Parliament should visit them; that inspection should ensure that those wrongfully detained were released and those rightly detained should be humanely treated; and that they should be supervised by doctors. It was many years before effective legislation converted these principles into practice. Dr JONES notes—and it is a thing true of every age—that the reformers themselves were not entirely aware, in these early days, of what they wished to achieve Perhaps, too, they were rather easily satisfied

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[1] Lunacy, Law and Conscience. By Mrs KATHLEEN JONES, PH.D. The International Library of Sociology and Social Reconstruction. London: Routledge & Kegan Paul. 1955. Pp. 231. 21s.

Much was being done outside Parliament Hospitals were being set up—St Luke's, London, in 1751, the Lunatic Hospital at Manchester in 1763, and the Retreat at York in 1792 In the first and last of these, gentle measures of treatment and occupation were advocated, and the Manchester Lunatic Hospital dealt more humanely with patients than was common at the time But the founding of asylums on a national scale began only with the County Asylums Act of 1808, which in turn followed the report of a select committee appointed in 1807 Amending Acts in 1811, 1815, and 1819 dealt with questions of admission, certification, and discharge of patients These took the responsibility for the admission of patients from the overseers of workhouses and placed it in the hands of magistrates, " thus weakening the connection of the county asylums with the Poor Law authorities "

Meanwhile Samuel Tuke had published, in 1813, his *Description of the Retreat*, setting out the " moral " management of the insane as practised there—management, that is, by gentle treatment and social activities Tuke, moreover, as a member of the Society of Friends, believed in the integrating influence of religion His patients were given no reason for feeling that their mental disorder cut them off from ordinary interests and activities The book was widely read, and when another select committee was set up, in 1815, public opinion was strongly with the reformers The committee found both law and practice in chaos At one end of the scale was the humanity of the Retreat, at the other the unspeakable barbarities of the private madhouses They published evidence of appalling conditions, dreadful neglect, and much cruelty Yet Bills to reform the private madhouses, introduced in 1816, 1817, and 1819, were all, after passing the Commons, rejected by the Lords, the main and most telling opponent being Lord Eldon, the Lord Chancellor After the third defeat the little band of reformers began to disintegrate the mentally ill had to wait on, year after year, for another champion

They found him in 1827, when a new select committee was appointed with Lord Ashley (afterwards Earl of Shaftesbury) among its members The committee introduced two Bills, both of which went through without difficulty the new County Asylums Act required visiting justices to send annual returns of admissions, discharges, and deaths to the Home Secretary, and the Madhouse Act placed the power of inspecting the Metropolitan houses in the hands of a statutory authority The 15 commissioners appointed under it were to visit without warning, and they had power to recommend that licences should be revoked The Act also required that a certificate for confinement of any patient should carry the signature of two doctors, as it does today An exception was made in the case of pauper patients, for whom the signature of one doctor, the parish overseer, and the incumbent, or of two justices, sufficed The new commissioners, who included Lord Ashley, worked so well that two years wrought a most striking change for the better in the Metropolitan madhouses As the years passed, the commissioners extended their interests they began to inquire into the characters and conduct of attendants and nurses, listened to patients' grievances and investigated them, and tried liberating recovered patients on trial In 1842 an Act was passed empowering the commissioners to pay a visit to every asylum and madhouse in the country The report on the first tour of inspection—" Ashley's report," Dr Jones says it may fairly be called—was published in 1844 and was the basis of the Lunatics Act, 1845 This gave the lunacy commissioners power to visit not merely the Metropolitan asylums and madhouses, but all county asylums and hospitals for the insane, and any other institution in which the insane might be found Bethlem—a much reformed Bethlem by this time—was deliberately excluded from such supervision. The Act also provided new methods of certification which decreased the risks of wrongful detention, and required better record-keeping Ashley believed in the value of documents as a safeguard against irregular practice The apathy and opposition which had defeated earlier Bills had disappeared the House of Commons was strongly in favour, and such opposition as there was came almost entirely from people who thought the Act did not go far enough

This is as far as Dr Jones's review of English legislation for the mentally ill takes us, but in an epilogue she reminds us of the landmarks of the last hundred years—the Lunacy (Consolidation) Act of 1890 (most of its provisions still apply to certified patients), the mental deficiency legislation of 1913–27, the Mental Treatment Act, 1930, and the National Health Service Act, 1946 Nor is the task of reformers in any sense finished A Royal Commission, headed by Lord Percy of Newcastle, set up last year, is considering the extent to which it is now, or should be made, statutorily possible for mentally ill or mentally defective people to be treated as voluntary patients without certification Northern Ireland[2] has already shown us that, by appropriate legislation certification, with all its attendant deprivations and legal disabilities, can be very largely avoided

The story of the change from gross superstitition and carelessness to a sense of responsibility for the mentally sick can be paralleled by several other developments in our social history over the past two hundred years Those who have read Sir David Henderson's Morison lecture,[3] however, will be struck again by the resemblance he sees between our attitude to the mentally ill and our attitude to " the behaviour and thought disorders which are indicative of abnormality and crime " Both the mentally sick and the socially undesirable are capable of rousing ugly responses in the rest of us we find it hard to keep in mind that an antisocial or otherwise troublesome person still counts as one, and not some negligible fraction Over the past two hundred years our response to the mentally sick has become progressively healthier and more mature, our reaction to criminals, too, has been maturing, though at a slower rate—being more primitive, as yet, by as much perhaps as a hundred years Of our progress in the mental field Dr Jones says " as we reach the point where history shades into present policy and future aspirations, we may derive confidence, if not complacency, from the achievements of the past two hundred years " Perhaps the same may be cautiously said of penal reform

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[2] *Lancet* 1954, i 1333

[3] Society and Criminal Conduct Edinburgh The Royal College of Physicians 1955 See *Lancet*, June 4 1955 p 1169

Annotations

REST AND ACTIVITY IN ACUTE NEPHRITIS

Akerrén and Lindgren[1] have been investigating the important question of how long strict bed rest is necessary for patients with acute hæmorrhagic nephritis They define the régime in the Children's Hospital at Gothenburg as rest in bed not only until possible 'general nephritic symptoms' such as increased blood pressure œdema, or raised N.P.N have disappeared but *also until the urinary findings* have returned to normal or practically normal. In questioning the need for this expensive routine, they were encouraged by finding that Czerny of Prague, had recorded in his memoirs in 1939 that children with acute nephritis who played in the streets recovered just as rapidly and completely as those who were made to rest From 1946 onwards Akerrén and Lindgren have treated alternate patients with (*a*) strict bed rest and (*b*) mobilisation as soon as macroscopic hæmaturia had disappeared Patients with recurrent attacks of hæmaturia associated with acute infection were later excluded, leaving 57 patients of whom 20 had been allowed to get up as soon as overt hæmaturia had disappeared. They found no noteworthy difference between the two groups Albuminuria and microscopic hæmaturia and increased sedimentation rate were not more persistent in the "up-and-about" group Tests of renal function gave similar results in the two groups and the length of time spent in hospital was rather shorter in the ambulant group Akerrén and Lindgren cite similar observations by Frisk and Klackenberg[2] and by Rudebeck.[3]

Early ambulation in acute nephritis, especially if it leads to earlier discharge from hospital is clearly of advantage to the community but it is not quite certain that thereby the patient is running no increased risk of chronic illness The present series was limited to children who do rather better than adults. Moreover there is some evidence that the attacks studied were very mild for of the 57 patients only 2 had tangible œdema and only 3 had hypertension Again there is no information about the delayed incidence of chronic nephritis. Acute type I nephritis though the ultimate prognosis is relatively good,[4] may be complicated by cardiac failure[5] by encephalopathy and by pulmonary œdema all of which require bed rest and some of which may outlast macroscopic hæmaturia. On the other hand no-one would want to keep patients with acute nephritis in bed until the last traces of albumin had disappeared, which might be at the Greek kalends A fall in blood pressure and a rise in urine volume—which may be abrupt[6] —are probably better signals for allowing the patient up than the disappearance of gross hæmaturia

RADIOGRAPHY OF THE COLON

RADIOGRAPHY can contribute much to the diagnosis of lesions of the colon especially those beyond the range of the sigmoidoscope But the radiologist often finds that the loops of the colon overlap and obscure each other so that inspection of a suspected area is very difficult and he may also be impeded by spasm or actual obstruction of the colon during the barium-enema examination The colon must be completely outlined in the filled state and all its tortuosities displayed then after the patient has evacuated his bowel it is highly desirable that enough of the barium shall remain to outline the mucosal pattern

It is not always easy to display the mucosal pattern of the colon Fischer[1] advocated for this purpose insufflation with air and Maingot et al[2] the use of thorium-oxide suspensions in place of barium sulphate Rigler[3] suggested in the early thirties that tannic acid should be added to the barium suspension but this method was widely adopted only in the late forties after Hamilton[4] and others had established a claim for it McLaren et al[5] have carried the search for an effective technique a stage further by using 'Veripaque' (dihydroxyphenylisatin) with a barium-sulphate suspension in which the particles are below 0·5 µ in size Veripaque is a colon stimulant, promoting rapid and complete evacuation and the colon can be observed radiographically as evacuation takes place through the enema tube after the colon has been completely filled McLaren et al say that with this substance the rate of colonic movements is suitable for accurate observation the contractions appear normal in character but increased in speed and vigour Apparently the increased rate of segmental and mass contractions is not associated with as much colic as may occur when tannic acid is used and McLaren et al claim that there are no contra-indications to the use of veripaque. From their experience they conclude that it aids study of structural detail and functional activity, and eases, for example, diagnosis of neoplasm and assessment of stenosis in regional ileitis involving the colon

DANGEROUS COTS

THREE children have died and one has narrowly escaped death as a result of accidents in their cots All the cots had bars close enough together to prevent the children from getting their heads between them and all the accidents were of the same type: the children slipped between the bars feet first and since their heads would not pass through, the weight of their bodies pulled their faces into the bedding and—except for the one rescued in time—they were smothered. In recent years the British Standards Institution (B.S.I.) have issued three standards for hospital and domestic cots, and two of these—issued in 1950 and 1951—recommended that cot bars in hospital metal cots should be 3–3¹/₂ in apart and those in domestic wooden cots not more than 3³/₄ in. apart. (Metal bars are less rigid than flat wooden bars, and hence may become slightly bent) The Ministry of Health and the Home Office were represented on the committees passing these standards—to which they have hitherto given their support In view of these accidents however they have felt obliged to consider the possibility that a standard devised to eliminate one type of accident may contribute to another type

In a Ministry of Health bulletin Dr Rachel Elliott and Mr W H Hammond[6] report that before the British Standards Institution was approached about altering these standards, two large health authorities (the London County Council and Birmingham County Borough Council) and a London pædiatrician were asked to collect measurements of babies and young children aged 6 months to 3 years Anteroposterior chest and pelvic measurements and head measurements made on some 600 children in L.C.C nurseries 600 in Birmingham nurseries and nearly 400 in London hospitals made it clear that a large proportion of children aged 18 months, greater numbers of younger children and even some 3 year-olds would be able to get their hips through a 3¹/₂ in space

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[1] Akerrén, Y Lindgren M. *Acta med scand* 1955 151 419
[2] Frisk A, Klackenberg G *Acta pædiat Stockh* 1945–46, 33 219
[3] Rudebeck J *Svenska Läkartidn* 1949 46 1
[4] Ellis A. *Lancet* 1942 i 1
[5] Peters, J P *Amer J Med* 1953 14 448
[6] Ross M. H *Quart J Med* 1950 19 161

[1] Fischer A W *Arch klin Chir* 1925 134 209
[2] Maingot G Sarasin R. Duclos, H Exploration radiologique des colons et de l appendice au moyen des solutions floculantes. Paris 1935
[3] Rigler, L Cited by Weber H M *Amer J Roentgenol* 1950 63 663
[4] Hamilton J B *Ibid* 1946 56 101
[5] McLaren J W King J B, Copland, W A *Brit J Radiol* 1955 28 245
[6] *Mon Bull Minist Hlth Lab Serv* 1955 14 [illegible]

The chest depth would prevent all but 1% of year old babies and 5% of 6-month babies from being able to squeeze through far enough to hang by the head, but the Ministry of Health rightly felt that in view of these findings the B S I should be asked to reconsider the standards The committee dealing with hospital cots did so, and—with full agreement between the medical representatives and the manufacturers—issued a new standard recommending bar spacing of $2^3/_4$–3 in, with an upward tolerance of $^1/_{16}$ in But unfortunately, the manufacturers of domestic wooden cots have not so far been persuaded to alter the bar spacing recommended in the existing standard The possibility of devising some kind of lattice work or mesh, which would get rid altogether of the need for bars and their hazards, does not seem to have been considered

The Folding Furniture Manufacturers' Association, whose members make 99% of babies' cots, claim that they have always put safety in the foreground of their policy, and that they have a record of fifty years of manufacture, at a rate exceeding 100,000 cots per annum, without a single fatal accident This is a good record, which they must surely be the last to wish to see broken It is therefore strange to find them arguing that the risk is only theoretical, depending upon the children being sufficiently emaciated to wriggle through the bars, and "able to contort themselves into the necessary sideways position, and upon the flesh over the buttocks, which was excluded from the measurements, not preventing passage" The 3 in specification, they say (taking a flight of their own into the realms of theory), "will lead to innumerable accidents such as fractures of arms, legs, &c" They add that the risk described by the Ministry of Health is "so remote as to be more than outweighed in terms of safety measurements", and that they would welcome an independent public inquiry

It is difficult to see how any further inquiry would help This is not a question of theory at all—of what kind of baby by what contortions could bring himself to an untimely end in this way It is a question of fact three children have already died from accidents in cots with bars so spaced that their bodies but not their heads could pass between them Surely the Folding Furniture Manufacturers' Association do not wish to wait until a child dies in this way in one of their own cots? Surely they would rather stand by their own policy and prevent even the possibility of another such disaster?

PERONEAL SPASTIC FLAT-FOOT

THE syndrome of spastic flat foot, with an eversion deformity, pain in the foot, and tightness of the tendons on the outer side, has still not been fully explained Bony abnormalities in this region contribute to the disorder[1 2], and in 17 affected feet Harris and Beath[3] found 15 abnormal bars, either between the calcaneum and navicular or between the talus and navicular With the special radiographic projections which are necessary to demonstrate the bar it became possible to separate those cases with primary bone defects, which were probably congenital, from those with arthritis in the subtaloid joint

Spastic flat-foot is almost exclusively confined to adolescents (the Canadian Army foot survey gives an incidence of 2%) and is much commoner in the male than in the female The height of the long arch is often unchanged, and the peroneal muscles, although prominent, may not be in spasm but merely show adaptive shortening Possibly spasm, when present, is due to an irritative focus in the subtaloid joint, while true shortening occurs in the presence of a bony deformity There is some evidence[4] that the everted position is the position of rest for the subtaloid joint This suggests that treatment directed towards the muscles, or towards correction of the everted position, is misconceived Tenotomy of the peronei, or division of their nerve supply, provides only temporary relief, since other muscles continue to produce the deformity Blockley[5] has shown that manipulation and immobilisation in plaster in the corrected position for three months also gives relief, but at the end of two years few patients were noticeably improved

In the treatment of patients with symptoms associated with bony bars, fusion of the subtaloid and talonavicular joints seems to be justified, although Webster and Roberts[6] have suggested that in young patients without arthritis a bar may be resected Only in the absence of a bony abnormality does conservative treatment offer a reasonable prospect of success

BIRTHDAY HONOURS

IT is a pleasure to record the high distinctions conferred on Sir Horace Evans and Sir John Charles for two kinds of service to the Crown, and the additional honour given to Sir Alexander Macgregor, whose work for Glasgow has continued since he ceased to be medical officer of health and became chairman of the Western Regional Hospital Board Of the new knights Mr Geoffrey Keynes, of St Bartholomew's Hospital, has contrived to be both man of letters and man of action as a surgeon, a scholar, and a person, he has long since been accorded knighthood in the minds of his fellows Next year he will be visiting Canada and Africa as a Sims Commonwealth travelling professor—an office held in 1952–53 by one of the thre new Australian knights, Prof H R Dew of Sydney, whose scientific reputation was first gained by his studies of hydatid disease and malignant disease of the testis Mr A E Coates, of Melbourne, is likewise a surgical teacher, with special experience of vascular surgery and with a record of war service extending from Gallipoli to Japanese prison camps, while Dr D R W Cowan consulting physician to the Royal Adelaide Hospital, is an authority on tuberculosis These are but a few of the notable names appearing in the list which we publish on p 1266—a list impressive once again in the immense range, both geographical and professional, of the valuable medical work it brings momentarily into view

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Dr D B BLACKLOCK, emeritus professor of tropical hygiene in the University of Liverpool at the Liverpool School of Tropical Medicine, died on June 10 at the age of 76

Dr REDCLIFFE SALAMAN, F R S, formerly director of the Potato Virus Research Station at Cambridge, died on June 12 at the age of 80

PRICE OF THE LANCET

As we announced with regret on April 23, the price of THE LANCET will be raised at the end of this month Any reader (at home or abroad) renewing his annual subscription on or after July 1 will be asked to pay £3 3s (reduced to £1 11s 6d for medical students, for doctors within a year of qualification and for those undertaking National Service in H M Forces) The rates for the air mail edition will be £1 1s higher than at present

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[1] Sloman N *J orthop Surg* 1921, 3, 586
[2] Badgley, C E *Arch Surg* 1927, 15, 75
[3] Harris, R I, Beath T *J Bone Jt Surg* 1948 30B, 624
[4] Lapidus, P W *Ibid* 1946, 28, 126
[5] Blockley, N J *Ibid*, 1955 37B, 191
[6] Webster, F S, Roberts, W M *J Amer med Ass* 1951, 146, 1099

Special Articles

THE YOUNG LONG-STAY PATIENT IN HOSPITAL

M. U. SHARP
M.A. Camb
MEMBER OF ASSOCIATION OF GENERAL AND FAMILY CASE WORKERS

At the request of the South East Metropolitan Regional Hospital Board, an investigation was made during 1953-54 into the position of young long-stay patients in hospitals in south-east London and the counties of Kent and East Sussex. The purpose was to discover how many such patients there were, and whether the hospital arrangements, so far as their welfare or social life was concerned, were adequate and satisfactory. The age range taken was 15–45 years inclusive, and the only illnesses excluded were pulmonary tuberculosis, carcinoma, epilepsy, blindness, mental defect, and psychosis.

INVESTIGATION

Thirty hospitals reported having in all a total of 96 patients (47 men and 49 women).

Of these, 17 (6 men and 11 women) were in acute wards, but only 13 were undergoing treatment; 31 (23 men and 8 women) were in wards for young chronic patients; and the remaining 48 (18 men and 30 women) were in wards for elderly chronic patients, where 3 of them were receiving treatment.

Of the 17 patients in acute wards, 13 were correctly placed according to their needs: 5 in the Chailey Heritage Craft School, 4 cases of poliomyelitis in appropriate hospitals, and 4 others undergoing active long-term treatment. The remaining 4 were untreatable.

Four hospitals, between them, have been able to accumulate [illegible] young patients together, often by exchanging them with elderly patients. This left 48 cases in wards for the elderly chronic sick, and 4 other cases in acute wards not receiving treatment, who could be regarded as being unsatisfactorily placed.

Most of the 96 patients have been in chronic sick wards for three years or more, 4 men and 1 woman having been in for over ten years each. No less than [illegible] of the patients (32 men and 37 women) fall into the age-groups 35–45 years; 12 (9 men and 3 women) were aged 15–24; and 15 (6 men and 9 women) were aged 25–34; 58 of the 96 cases (60%) suffered from diseases of the nervous system, of which disseminated sclerosis was the commonest, with 12 men and 15 women. Diseases of the bones and joints and muscles accounted for 13 cases, infective and parasitic diseases for 11, and congenital malformations for 7.

PROPOSED DISPOSAL

There were 52 young patients for whom more satisfactory arrangements could be made. No immediate change could be offered, but attempts were made to discover what their own wishes were. It was found that 24 (8 men and 16 women) would like to be moved, while 21 (12 men and 9 women) would prefer to remain where they were. A further 4 women were in any case too ill for transfer, and 3 women were undergoing treatment in chronic wards for the elderly.

The immediate need is thus to find some happy solution for the 24 patients who wish to be moved; but it would be wrong to write off the others as happy and satisfied with their surroundings. The reasons given for not wishing to be moved were: nearness to relatives (10); a preference for the known to the unknown (9); a wish not to lose the friendship of the patient in the next bed (2). This does not necessarily imply that the best is being done for these patients, or that they would not have chosen to go elsewhere had a more suitable offer been made at the time of admission.

The solution for those who wish for a move does not lie in providing wards for 8 men and 16 women: the problem is far more complex. The 8 men are at present in eight hospitals and the 16 women are in ten hospitals scattered throughout the region. In only two instances are any 2 of the women in the same ward; for some are light and some are heavy cases and they are distributed accordingly. Again, patients who wish to leave their present surroundings do not all wish to be far removed from their home district. It must also be borne in mind that patients in the early stages of disseminated sclerosis would find it very depressing to be close beside those in the advanced stages. It would be easy, too, for someone with a difficult or abusive temperament to wreck the happy atmosphere of a ward. Care must therefore be taken in the initial stages of building up any unit for the young.

But it would not be right to emphasise the difficulties without also stressing the urgent need for better provisions for these young patients. Two case histories may speak for all.

Case 1.—A spastic of 38, severely handicapped in his legs but with use of his hands and very alert mentally. His father was a professional man, and he was used to life in a comfortable home until he was placed in a sheltered workshop. He was later transferred to the chronic ward, to be the only young one among the old men, with no outlet for his intellectual interests, and only handicrafts with which to occupy his time.

Case 2.—A woman of 25, bedfast with disseminated sclerosis, who, because of the degree of nursing care required, is placed in the ward with the very elderly and senile patients. Her hands are too shaky to do more than a little knitting, and her sight is too much affected to make reading possible. She is beset with worries about her husband and small boy at home, and has nothing to take her mind off her troubles as she gazes idly round the dreary ward full of those nearing their journey's end.

THE SCHOOL-LEAVER

The Ministries of Health and of Education combine to offer the severely handicapped child nursing, and schooling in a suitable environment; but what provision is there for him if further institutional care is essential, or if his home is inadequate to deal with his needs when he has to leave at the age of 16? Is the chronic ward the only answer which the Welfare State can give?

Case 3.—A boy was at grammar school when he caught poliomyelitis; it left him paralysed in all limbs, with the exception of his right foot, tips of fingers, neck and head muscles. Much effort was necessary before he would face life again and find in it some compensation for all he had lost. He can write now with a pen in his mouth and is learning remote-control typing, and it is possible that he may be able to sit for part of his General Certificate of Education shortly. But what of his ultimate future? Where can he go in order that he may use his intellectual gifts, since illness has deprived him of his physical powers?

I made some further inquiries both from education authorities and from voluntary bodies which specially cater for the education of handicapped children, and I found 9 severely handicapped children aged 15–16 years who are receiving special-school education. It is thought that 6 of them will be unable to receive sufficient care at home on leaving school, the cases of the other 3 being doubtful. In addition I found 5 16-year-olds in hospitals in this region, and a further 4, belonging to this region, in the children's hospital of a neighbouring region. These 18 young people suffer from a variety of diseases: muscular dystrophy (5 boys); cerebral palsy (2 boys, 2 girls); poliomyelitis (1 boy, 2 girls); fragilitas ossium (2 girls); spina bifida (2 boys); hydrocephalus (1 boy); Friedreich's ataxia (1 boy).

Of 8 difficult placement cases who left Chailey Heritage in the last three years, 3 went to other hospitals for further treatment, and 5 to accommodation provided by voluntary societies. This may sometimes be the best solution, but there is a great lack of such voluntary homes, and the waiting-lists are long

A spastic girl of 16, leaving a special school, was sent into a private hospital run by a sisterhood, and a boy with spina bifida has been in a chronic ward for four years, since he left school Yet another, with muscular dystrophy, now aged 18, has been in a chronic ward for two years, but fortunately with a few others aged 16–45 This hospital has accepted another muscular dystrophy patient aged 16

All in close touch with this problem are concerned at the lack of suitable provision for this class of youngster

POTENTIAL LONG STAY PATIENTS

During 1952–53 I made a survey, under the Leverhulme Research Awards, into the social problems of disabled persons living in Kent, in the 15–45 age-groups Of 340 persons visited in their own homes, I found 42, aged 25–45, who either by reason of failing relatives or of progressive disease, might be expected to require hospital admission within the next five years Of the 42, 19 were cases of disseminated sclerosis, and another 10 had other progressive diseases, 20 of the 42 were living with elderly parents, and 3 were living alone, the others were looked after by husband or wife

Older patients (aged 45–55) in chronic wards also deserve attention, especially those who are mentally alert 11 men and 23 women were specially referred to me because of their mental alertness, and there would undoubtedly have been more had I been looking for them If in planning for the future these patients are considered, with the younger ones, the numbers to be catered for will be much higher than those suggested by this survey

DISCUSSION

Young long stay patients are not only patients they are also human beings with diverse needs in the way of companionship, interest, occupation, and (perhaps the most fundamental need of all) the feeling of being "wanted" and of being some use in the world

I found that doctors, nurses, and almoners all agreed that it is not right to allow the young to remain indiscriminately with the old, but there was no uniform opinion as to how the problem should be tackled There is little, if any, spare money to use in the creation of anything new A few hospital management committees have made a start by gathering the younger patients together in one ward, often by exchange with older patients, but this in itself creates difficulties because such young patients are likely to occupy their beds for many years, hence they reduce the number of active beds in the hospital

In other hospitals the answer has been to place the patients in acute beds, but should the prevailing atmosphere, for the long-stay patient, be that of a busy acute ward? In chronic wards, however, he is usually surrounded by the old, the incontinent, and the dying The fact that one man, now aged 40, has become so used to his surroundings, after thirty bedfast years, that he does not want to be moved, does not prove that present accommodation is adequate but rather it shows that the power of adjustment in human beings is infinite

What type of accommodation is most suitable for the young long stay patient and what is available for him? What better use can we make of the resources at our disposal?

Is the answer to be found by grouping the young together within the curtilage of a general hospital with full ancillary services, where they have the chance of active treatment and rehabilitation? But what if this ends in transfer, within the same hospital, to a geriatric ward when the "young" grow "old"? Is it possible to bring in even more outside life than is at present done, so that the young patient may feel he belongs to the community outside, not only through their visits to him, but by his excursions into the normal world of social life, sport, and church worship? If that is the answer, should there be several small units in each region, to allow of reasonable access by relatives? Or should there only be one or two, in which resources can be pooled? How is a balance to be struck between the needs of the "difficult" and the very ill patient, and those of the other patients in a ward? Is a person to be judged as "young" by his date of birth or by his mental alertness, and at what age does he become "old"? What can be offered to the 16-year old? Are there any improvements which could be introduced, here and now, by those hospitals which already accommodate young long stay patients?

Finally, is this problem so widespread, that it should be considered for the country as a whole instead of being tackled by hospital management committees and regional hospital boards? Though widespread, it is perhaps not a large problem it need not call for the expenditure of large sums of money But it does call for the free use of knowledge and imagination so that these young long stay patients may have some chance to live the richer, fuller life which is surely their due

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"MINOR" ADDICTIONS

Barbiturates, Methylpentynol, Tobacco

On May 23 the Ciba Foundation devoted a quarterly clinical forum to Major Consequences of Minor Addictions

Dr H **Pullar Strecker** (hon secretary, Society for the Study of Addiction) said that the World Healt Organisation's expert committee in 1950 and 195 recognised three groups of drugs

1 *Addiction producing*—Some drugs (notably morphine have a specific pharmacological action which will alway produce compulsive craving, dependence, and addiction u anybody With these drugs pharmacological action is paramount, psychological make up adjuvant Such drugs caus individual and sociological damage

2 *Habit-forming*—Other drugs never produce compulsiv craving, yet their pharmacological action is found desirable t some individuals to the point that they readily form a habi of administration—a habituation Administration can b interrupted without significant disturbances With them th psychological make-up is paramount, pharmacological actio adjuvant They cause no sociological damage

3 *Intermediate*—The pharmacological action of some drug is intermediate in kind and degree between groups 1 and 2 Compulsive craving, dependence, and addiction can develo in persons whose psychological make up leads them to see and find escape in drugs Psychological make up is th determining factor, but pharmacological action plays significant rôle

He himself prefers to classify them as (1) essentially malign, such as narcotics, (2) potentially malign, such as barbiturates and alcohol, and (3) essentially benign, such as tobacco But they can be compared according to various different criteria For instance, in terms of what people will pay to get their drug, narcotics come first, with tobacco a close second on the Continent after the late war there was hardly anything people would not and did not give in exchange for cigarettes But the hallmark of an addiction is the suffering entailed when it is unobtainable, which is worst with narcotics and really quite bearable with tobacco Another criterion is the difficulty entailed in discontinuing the drug by one's own unaided efforts—a difficulty by no means insuperable with tobacco In social effects—the extent to which it cuts across family life, work, duties, obligations, reputations, and so on—alcohol is easily worst, followed by narcotics and barbiturates Tobacco does not figure here at all, and that is why, not so long ago, we were rejoicing over the inroads that tobacco was making on the consumption of drink (Since 1900 the consumption of tobacco has increased two and a half times and the consumption of alcohol has decreased to about half) But unfortunately now that the connection between smoking and lung cancer has become well nigh inescapable, tobacco has displaced alcohol as the greatest danger to public health. By this criterion alcohol now takes second place, with barbiturates as the runner up Narcotics—perhaps because they are so well controlled in this country or perhaps because the British as a nation are not given to addiction—is no public health problem in this country

But how Dr Pullar-Strecker asked can the powers that-be afford to discourage smoking when it brings the State £030 million a year in revenue—more than enough to defray the nation s entire health services ? One suggestion might be to increase the taxation on pools and other forms of gambling measured against the physical corruption of lung cancer the supposed moral corruption of gambling appears almost a blessing but the money obtainable would he thought, be relatively negligible. In the fight against excessive drinking much has been done by taxation closing hours and counter attractions; but tobacco consumption would comfortably withstand a further increase in taxation and the other remedies are inapplicable. There remains education, by which it might be possible to induce young people not to take up smoking This should be done not so much by emphasising the potential danger as by making non-smoking worth their while. In this world you cannot make people think as you do but you can make it worth their while to do as you think. With those who are smokers already, education will cut little ice

BARBITURATE ADDICTION

Dr R. A. **Hunter** (York Clinic, Guy s Hospital) said that this century has seen a tremendous increase in awareness of psychiatric conditions, without an equivalent increase in psychiatric understanding The general practitioner is in the unhappy position of being taught to recognise conditions which he is powerless to treat What is he to do about the 50–75% of his patients whose symptoms seem to have their origin in the mind or emotional life ? The answer of course is drugs—sedatives, hypnotics, and stimulants In the U.S.A in 1048 enough barbiturate was manufactured to provide every inhabitant with about 30 grams a year In this country in 1919 almost 10% of all the drugs prescribed under the National Health Service were barbiturates, and today 15% would be nearer the mark It is therefore surprising that the dangers of this group of drugs are so little recognised.

A great deal of chronic invalidism is caused by the liberal prescription of barbiturates for minor physical and psychiatric symptoms, because suppression of symptoms is mistaken for treatment In milder cases with regular dosage and unfailing supplies withdrawal symptoms hardly appear; but if they do it is in the form of exacerbation of the original symptoms for which the drugs were prescribed and accordingly their significance as signs of a barbiturate habit is not appreciated by either doctor or patient. Though it has been thought that tolerance to barbiturates does not develop its existence is shown by the many patients who take barbiturates in hypnotic doses in the daytime without producing sleep—simply in order to keep going Psychical dependence will develop in about a month if the patient is given a barbiturate at night with two or three smaller doses during the day Physical dependence is best demonstrated by abrupt withdrawal of the drug sometimes undertaken on admission to hospital so that the patient's psychiatric condition can be followed without masking of the symptoms by drugs. In patients who have been on barbiturates such withdrawal may cause insomnia for as long as five days besides severe anxiety symptoms But once over this stage many are well enough to leave hospital in the words of Sir Samuel Wilks " the mere absence of treatment by physic is often a positive stage towards cure "

Many patients and their doctors are not aware that the original symptoms are maintained by the treatment While the barbiturates act, these symptoms are inhibited but each time the effect wears off they return At first it is only the contrast between being with and without the symptoms that makes the patient go on taking the drug but in time the symptoms of abstinence are added, so that when the drug wears off the patient is left with his original depression, insomnia, and anxiety, plus the same symptoms produced by the temporary withdrawal of barbiturates in the intervals between doses. The vicious circle of increasing and more frequent doses has started and finally the confusion of barbiturate intoxication is superadded Thus a mild psychiatric disturbance, amenable to one or two psychotherapeutic interviews is converted into a serious condition Patients who would not otherwise have done so may be driven to attempt suicide and are at this stage often diagnosed as suffering from endogenous depression and subjected to electro convulsions If the cause remains unrecognised leucotomy may be performed for what was originally an iatrogenic state of barbiturate intoxication, or a state of addiction which went unrecognised.

In conclusion Dr Hunter said that " to assess the danger of barbiturates is not to despise them I would simply plead for fewer drugs and more understanding of the patient s mind."

STIMULANTS AND DEPRESSANTS

Dr A D **Macdonald** (professor of pharmacology, Manchester) thought it would be odd if the synthetic chemist did not try to produce better stimulants and more controllable depressants than the caffeine and alcohol so long used by mankind

Among stimulants the amphetamines stand out head and shoulders: their value against fatigue and mild depression has been established and the likelihood of addiction is lessened by their being more efficient when used occasionally than when used regularly Amphetamine is also offered in combination with phenobarbitone and mephenesin, and these cocktails in tablets have fascinating pharmacological possibilities The presence of schedule IV poisons does not prevent a demand for them with which the manufacturers (he was told) cannot keep pace

Methylpentynol was introduced in America in 1951 as a short acting hypnotic but is now advertised here for the " emergencies " of daily life—public speaking interviews examinations, visits to the dentist. Trotter[1] reported that in the recommended dosage its effect on behaviour was negligible. Similarly in a test of accuracy in adding numbers Professor Macdonald found on the average, little change—performance being 5% better after amphetamine (10 mg) 6% worse after alcohol (2 oz 40% *v/v*) and 8% worse after methylpentynol (500 mg) But in two out of fifty students performance was 40% worse after methylpentynol, and in a test with dummy capsules he found it easy to tell which students had had the drug People who take the drug may exceed the recommended dose and it is not surprising that there have already been charges of car-driving under the influence. A young man who took seven capsules awaits trial for manslaughter Yet the drug is still unscheduled and advertised as safe and harmless

The potential value of drugs which will relieve anxiety states and even the milder forms of nervous tension is enormous said Professor Macdonald But in his opinion their use and advertisement without medical control and without restriction is to be deplored

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[1] Trotter P *Lancet* 1951 ii 130.

TOBACCO

Miss **Flora Beck** (almoner, General Infirmary, Leeds) said that for the occasional smoker the aroma of tobacco and a faint dulling of emotional awareness provide a small distinctive addition to the pleasures of relaxation, but the physical and emotional effect is small. Under social pressure, however, it is easy to become acclimatised to smoking more heavily, and after a day's abstinence the first cigarette gives a feeling of physical and emotional relief of a kind and degree which is new. At this stage the body has readjusted to neutralise the effect of a constant overdose of nicotine; to go without smoking upsets what has become its normal state, and an artificial craving has been induced. Satisfaction of this craving gives a feeling similar to the normal satisfaction of some primary need; and where deprivation and frustration are present they can be superficially allayed in this way.

> "A need for affection, a need for food, a need for physical activity, a need for rest, a need for intellectual stimulus, a stirring of the spirit—all these, after a time, may be falsely decoded in the mind and presented to consciousness as one single simple cry: 'I want a cigarette.' The cigarette does give satisfaction. The duped conscious mind assumes that all is well. . . . In this way a tiny physical 'addiction' can become the focus for powerful inner drives—and it deflects them away from the constructive attempt to satisfy real needs."

Mass addiction to tobacco represents a vast drain on personal and national income, and does much to perpetuate the ills it claims to relieve. What can be done about it? The example of light smokers or non-smokers carries more conviction with the average smoker than rabid anti-smoking speeches. Though it is important to broadcast the dangers of smoking, this should be done rather to reinforce a positive policy than to frighten people off. Life is *pleasanter* when freed. A general trend in public opinion slightly against smoking would have a big effect, and in a general campaign the person to aim at is the "floating smoker."

The really habituated smoker, if he is to change, must *want* to control or give up smoking. He may then adopt one of three methods:

1. *Cut off completely and for good.*—Some do this and after a few weeks are no longer bothered at all. But where a psychological urge has been built up, this method may leave a permanent feeling that some tremendous pleasure has been renounced. This may bring fear of relapse, and the whole subject of smoking remains disturbing.

2. *Reduce by rationing.*—This needs a less drastic act of will at the start but constant lesser self-control. After readjustment, physical craving will be satisfied at a lower level.

3. *Start by stopping completely (if possible for at least three weeks), then smoke for a few days and give it up again.*[2]—During abstinence, when the physical craving has died down, the psychological urge is still building up. Smoking comes as an anticlimax: the expected strong satisfaction is not felt, and will not be, unless smoking is continued long enough to induce a physical craving again. It takes numerous repetitions of this to undo the conditioning which associates smoking with strong satisfaction; but the tendency to translate any inner tension into the feeling "I want to smoke" gradually dies out.

Whereas the mild physical "addiction" to smoking can be cured in a few weeks, it takes months or even years to rub out the mental habit pattern. "It is obviously much better," said Miss Beck, "never to become addicted. Those who take care not to exceed 10–15 cigarettes a week can safely enjoy smoking, if they wish, without fear of the habit taking charge."

In the discussion Dr. **Horace Joules** said that, though it is estimated that a million people in England and Wales will die from carcinoma of the bronchus before the end of the century, he is even more concerned at the 30,000 deaths annually from chronic bronchitis preceded by long years of discomfort and disability, which would be largely prevented if people would stop smoking. He accused the Ministry of Health of failing to tell the public about the harmful effect of tobacco, and he praised the *Journal of the American Medical Association* for refusing to accept tobacco advertisements. Prof. F. R. **Winton** spoke of the difficulty of preventing maladjustment and frustration in people who find life in modern communities unsatisfying, and referred to the decline of religious institutions. Addictions would vanish if psychiatrists could cure the disorders underlying them. Prof. W. D. M. **Paton** questioned whether we are tinkering with the surface of a deep human need, which would express itself in some other way if addiction were abolished. We should address ourselves to the nature of this fundamental need. Dr. A. **Levene** thought it would be instructive to make a study of the 10% of people *not* addicted to tobacco. Addiction to barbiturates or to methylpentynol is doctor-made, and therefore a different problem from smoking. Dr. **Keith Simpson** said that, given the opportunity, any nation is a nation of addicts. Tobacco and alcohol are minor addictions in adolescence, but may lead to major addictions such as marihuana, "goof pills," or heroin. Experience has shown that placing a drug on schedules I or IV cannot be relied on to prevent its abuse. Dr. **Pullar Strecker** referred to the addition of ipecacuanha to barbiturates, so that an overdose will cause vomiting, and predicted that pharmacologists will eventually devise means of making barbiturates addiction-proof.

BIRTHDAY HONOURS

The list of honours published on June 9 contains the names of the following members of the medical profession:

G.C.V.O.

Sir **Horace Evans**, K.C.V.O., M.D. Lond., F.R.C.P.
Physician to H.M. the Queen.

K.C.B.

Sir **John Charles**, M.D. Durh., F.R.C.P.
Chief medical officer, Ministry of Health, Ministry of Education, and Home Office.

K.B.E.

Sir **Alexander Macgregor**, O.B.E., M.D., LL.D. Glasg., F.R.F.P.S., J.P.
For services to public health in Scotland.

Knights Bachelor

Albert Ernest Coates, O.B.E., M.D., M.S. Melb., F.R.A.C.S.
Stewart lecturer in surgery, University of Melbourne.
Darcy Rivers Warren Cowan, M.B. Adelaide, F.R.A.C.P.
Consulting physician to the Royal Adelaide Hospital.
Harold Robert Dew, M.B. Melb., F.R.C.S., F.R.A.C.S.
Professor of surgery, University of Sydney.
Geoffrey Langdon Keynes, M.D. Lond., F.R.C.P., F.R.C.S., F.R.C.O.G.
Consulting surgeon, St. Bartholomew's Hospital.

C.B. (Military)

Surgeon Rear-Admiral **Seymour Grome Rainsford**, D.S.C., M.D. Dubl.
Major-General **Albert Sachs**, C.B.E., M.D. Dubl., M.R.C.P., Q.H.P., late R.A.M.C.

C.B. (Civil)

Walter Eric Chiesman, M.D. Camb., F.R.C.P.
Medical adviser, H.M. Treasury.

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[2] In first describing this method (*Lancet*, 1953, ii, 392) Miss Beck recommended that after the period of abstinence, one should smoke so heavily as to induce aversion. This she now thinks unnecessary.

C.M G

Benjamin Keith Rank M.S Melb F.R C S F.R.A C S
Chief plastic surgeon Heidelberg Military Hospital Victoria

Allan Robert Stanley Vickers O.B E CH.M Sydney
For services to the Flying Doctor Service in Australia

C B E (Military)

Air Commodore Albert Frederick Cook, O.B.E L.R C.P.I

Brigadier Allen Lepard Crockford D.S O., O.B E M C M.B Camb., Q.H.S late R.A.M C T A

C B E (Civil)

Roger Gilbert Bannister, M.R.C.S
For services to amateur athletics.

Philippe Leslie Caro Carrier, M D Lond M.R.C.P
Senior medical officer Home Office

Charles William Atkinson Emery M.B Belf
Principal medical officer Ministry of Pensions and National Insurance

Mary Esslemont LL.D M.B Aberd J P
General practitioner in Aberdeen for services to medicine in Scotland.

Edward Thomas Bondfield Green M D
Senior bacteriologist, Institute for Medical Research Federation of Malaya.

Ewen Lewers Grove M D Melb F.R.A C P
Physician, Launceston Hospital Tasmania

Ivan Arthur Llewelyn Vaughan Jones M.B Glasg J.P
For services to the Ministry of Labour and National Service.

William Caldwell McClelland M.B Melb
For services to sport in Australia.

Frederick Grantley Morgan M.B Melb F R.A C.P
Director Commonwealth Serum Laboratories, Victoria

Frederick William Roques M CHIR. Camb F R.C.S F.R.C O G
Consultant in gynæcology to the R.A.F obstetrician and gynæcological surgeon Middlesex Hospital

Sir Leonard Rosenheim, M.D Camb F.R.C.P
Professor of medicine in the University of London at University College Hospital.

James Leslie Allan Will, M.B N.Z. F.R C.S E., F.R.A C.S
Orthopædic surgeon Christchurch General Hospital.

M V O (4th class)

Lieut.-Colonel William Hilgrove Leslie McCarthy D.S O M.C. M.D Dubl. M.R C.P

O B E (Military)

Lieut.-Colonel George Gregg M.D Belf., F R.C P.I , R.A M.C T.A

Lieut Colonel William Muir Stewart M B Belf R.A M C

Wing Commander Alistair Robert Cameron Young M.R.C.S., R.A.F

O B E (Civil)

William Roy Billington M D Camb
For medical services in Uganda.

Arthur Douglas Briggs M.B Glasg
Medical superintendent Stobhill Hospital Glasgow

David Eric Cameron Mekie M D Edin F R.C.S.E.
Professor of surgery University of Malaya.

Edwin Ekevuo Onwu M.B Edin
Deputy director of medical services eastern region Nigeria.

Edwin Alfred Trim M D Camb
Deputy director of medical services Kenya

M B E (Military)

Major Clark Nicholson M C M D Glasg R.A M C T.A.

Squadron Leader Charles Geoffrey White B M Oxfd. R.A.F

M B E (Civil)

Neville George David Campbell, B.M Oxfd
Medical officer Sierra Leone

Donald Gordon Duff M C M B Edin., F.R C S E
Surgeon superintendent Belford Hospital Fort William

Lyell Maurice Barkley Hill, M B Belf
Regional medical officer British European Airways.

Alex Todd M C., D F C., M B Edin
For medical and missionary services in Northern Rhodesia.

Public Health

LYMPHOCYTIC MENINGO-ENCEPHALITIS IN THE MANCHESTER AREA

J O'H Tobin
B.M Oxfd Dip Bact

LECTURER IN BACTERIOLOGY UNIVERSITY OF MANCHESTER

Lymphocytic meningo-encephalitis (L.M E) is a syndrome which is due to many different micro organisms and which has been known by a variety of names since Wallgren in 1924 first drew attention to it as aseptic meningitis.' The six well known criteria laid down by him for its recognition have been modified as knowledge of the syndrome has increased and as agents producing similar but clinically distinguishable features have been demonstrated Wallgren (1951) noted over 20 viruses, spirochætes yeasts and protozoa as causes of L.M.E Viruses are involved most often in this syndrome, poliomyelitis being generally considered the most important However a large proportion of cases diagnosed as non paralytic poliomyelitis, even during an epidemic of this disease are due to other identified and unidentified agents (Tobin et al 1954)

Simple serological procedures are available for the diagnosis of infection with the widespread lymphocytic choriomeningitis, herpes simplex and mumps viruses for the leptospiræ and for certain of the arthropod borne varieties of encephalitis in those areas where they are known to occur More extensive tests are required for the diagnosis of poliomyelitis Coxsackie and other viruses.

Few reports give any real picture of the incidence of the L.M.E syndrome or of its ætiological agents, because figures are based on selected groups of the population often scattered over large areas Until L M.E is made notifiable any exact idea of its incidence will be unobtainable at present it is necessary to draw inferences from those cases admitted to hospitals or from samples tested in virus laboratories (Afzelius Alm 1951 Adair et al 1953 Virus Reference Laboratory 1953, Gard 1954 Nilsby 1954) In this paper the results are reported of investigations on the viral ætiology of L.M.E in one area served by a small virus laboratory

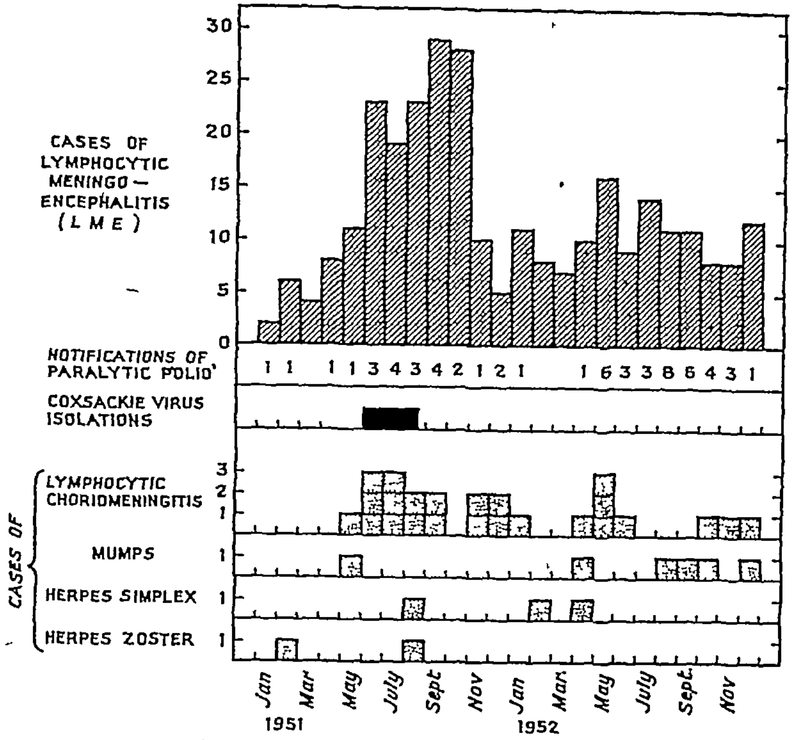
Laboratory Investigations

During 1951–52 samples for virus investigation were received from 201 patients in the Manchester area who were diagnosed as having non paralytic poliomyelitis, aseptic meningitis, lymphocytic or serous meningitis, meningo-encephalitis, encephalitis, and choriomeningitis. As meningitis and encephalitis in such cases rarely occur separately and as the pleocytosis in the C.S.F is predominantly lymphocytic these syndromes have been referred to in this paper as *lymphocytic meningo encephalitis*

Samples were received throughout both years with a peak during the summer and autumn of 1951 when the syndrome was encountered more frequently than normal by local physicians The number of patients from whom specimens were received is illustrated by the accompanying figure which also indicates when cases due to the test viruses occurred Each patient was investigated for the rôle of one or more of the following viruses in the ætiology of this syndrome

Lymphocytic Choriomeningitis

201 cases were examined by the complement fixation technique for specific antibody to this virus and occasionally by attempted isolation or by serum neutralisation tests in mice A diagnosis of this disease, which can often be made on *clinical and epidemiological grounds* with considerable assurance was accepted as being confirmed by either (1) a rising titre of complement



Monthly distribution of patients investigated

fixing or neutralising antibody, or (2) the presence of complement fixing antibody together with isolation of virus from the cerebrospinal fluid, blood, or throat washings 15 cases due to this virus were diagnosed in 1951 and 9 in 1952, 20 being in adults over fifteen years of age and 4 in children

Mumps

273 cases were examined by either the complement-fixation test using allantoic fluid as source of virus antigen, or in a few cases by the hæmagglutination inhibition test A fourfold rise in antibody titre was considered diagnostic of this infection in two samples of serum, one taken during the acute phase and another during convalescence Only 6 cases were due to this virus, but, as material was received only from patients who developed parotitis after the onset of the neurological signs or who had no parotitis, some cases may have been missed owing to lack of requests for serological confirmation 2 cases were in adults and 4 in children

Herpes Simplex

124 of the cases were investigated by the complement-fixation test using either antigen prepared from the chorio allantoic membrane of infected chick embryos or from infected allantoic or amniotic fluid. The majority of these tests were kindly done by Dr N L Modi This test was used as a screen and a rising titre confirmed by the neutralisation test using the chorio allantois of the developing chick embryo About 15% of the sera reacted non specifically with normal chorio allantoic extracts, and these were also tested for antibody by the neutralisation technique. 3 cases, 2 in children and 1 in an adult, were found to be due to infection with this virus

RESULTS OF VIRUS INVESTIGATIONS ON 291 CASES OF LYMPHOCYTIC MENINGO ENCEPHALITIS

Test virus	No of cases investigated			No of cases positive			% of cases positive		
	Total	15 yr or over	Under 15 yr	Total	15 yr or over	Under 15 yr	Total	15 yr or over	Under 15 yr
Lymphocytic chorio-meningitis	291	152	139	24	20	4	8 4	13 2	2 9
Mumps	273	143	130	6	2	4	2 2	1 4	3 1
Herpes simplex	124	61	63	3*	1	2	2 4	1 7	3 2
Encephalomyocarditis	41	22	19	0	0	0	0	0	0
Coxsackie†	62	8	54	4	0	4	6 5	0	7 5

* Including one case from which a " C " virus was also isolated
† Diagnosed by virus isolation or rise in specific antibody

Encephalomyocarditis Group

41 sera were tested by the neutralisation technique using 100 ID_{50} doses of MM virus, the serum virus mixtures being given by the intraperitoneal route in mice In no case were antibodies to this virus found

Coxsackie

During the summers and autumns of this period, one or more fæcal samples from 62 cases were investigated for " C " virus by the inoculation, either subcutaneously and/or intracerebrally, of suckling mice less than twenty four hours old Only 5 strains of virus were isolated from the 47 patients studied in 1951, and none from those in 1952 These were isolated from 4 patients, one being infected simultaneously with 2 " C " virus strains and another who had a concurrent primary herpes simplex encephalitis Another patient showed a significant rise in antibody to one of the " C " viruses during her illness 3 group-B type 3 strains were found and 2 group A, types 2 and 4, the latter being those associated with the dual infections

Herpes Zoster

Although no methods were known for the cultivation of herpes zoster virus in our laboratory at that time (Weller 1953), sera from 2 cases of herpes zoster with L M.E were investigated to exclude herpes simplex virus infection, because this virus has been isolated from zonal lesions (Beeuwkes 1939)

The above results are summarised in the table

Discussion

In this series the proportion of cases shown to be due to specific viruses was small Lymphocytic chorio-meningitis, herpes simplex, and mumps infection accounted for approximately 7% of the cases in children and 16 5% in adults, while none was found to be due to the encephalomyocarditis group of viruses. Lymphocytic choriomeningitis was associated with the two localised endemic areas in Manchester noted by Duncan et al (1951) Cases of this disease were generally clinically distinct from the other cases of L M E in having a prodromal phase before the onset of meningitis and a considerable proportion of them having a low level of sugar in the cerebrospinal fluid, a finding observed by Duncan et al (1951) and confirmed in the recent report of Adair et al (1953) from the United States The mumps cases, as would be expected, occurred when the disease was most prevalent Although 3 cases of herpes simplex infection occurred, this virus, and that of mumps, did not seem to cause as high a percentage of cases as in the series recorded by the American workers

The work of Curnen et al (1949) and Gabinus et al (1952) has indicated that the B group of the Coxsackie viruses can cause L.M.E and these viruses have been recovered from the cerebrospinal fluid of patients on two occasions (Gabinus et al. 1952, Hummeler et al 1954)

Gard (1954) thinks that they are responsible for a large proportion of the cases of this syndrome in Sweden However, no evidence could be found to suggest that they played any but a very small part as causal agents of L.M.E. in the Manchester area in 1951 when C viruses were known to be prevalent (Bury and Tobin 1952)

In 1951 the C virus isolations both from meningo encephalitis and Bornholm disease cases occurred before the L.M.E. reached its peak and both Gard (1954) and ...unen (1952) have noted that infections with these ...ruses may anticipate the poliomyelitis season ...eutralisation tests with the types of C' virus isolated ...d with three other types on the sera of patients ill in ...ugust to November confirmed that lack of isolation of ...ese viruses then was due to their absence in the patients ...sted

Lymphocytic choriomeningitis occurred more fre...ently in adults than in children—young housewives ...ing the most usual victims—while the Coxsackie ...uses were isolated from those in the younger age group ...erological studies using the HeLa cell-culture method ...cribed by Syverton et al. (1954) showed that polio...elitis infection was present in the area Of 11 indivi...uals tested 10 had antibody to type 1 9 to type 2 ...d , to type-3 poliomyelitis virus However only ... cases of paralytic disease were reported from South ...ast Lancashire in 1951 and 35 in 1952 The exact ...lationship of these viruses to L.M.E cannot be decided ...til we know the results of investigations now in progress ...Although L.M.E seemed to be more prevalent during ... summer and autumn a large proportion of the cases ...this series occurred during the winter and spring, ... until this syndrome is made notifiable much of its ...idemiology will be shrouded in obscurity

Thanks are due to the many physicians who sent in sera ...m patients under their care to Dr Sven Gard for the ... virus and to Mrs. B M Snape for her valuable technical ...sistance

REFERENCES

...b, C. V Gauld R. C. Smadel J E. (1953) *Ann intern. Med* 39 675
...Alm, L. (1951) *Acta med. scand* suppl 263
...ken, H (1939) *Schweiz Z allg Path.* 2, 334
... J. H. B., Tobin, J O H (1952) *Lancet* ii, 207
...s, E. C. (1952) Poliomyelitis: Papers presented at the 2nd International Poliomyelitis Conference, London, p 1°1
...haw, E. W Melnick, J L (1949) *J Amer med. Ass* 141 894
...m, P H, Thomas A. E. Tobin J O H (1951) *Lancet*, i 956
...s, O., Gard S Johnsson, T Poldre A (1952) *Arch ges Virusforsch.* 5 1
...S. (1954) *Ji Lancet* 74, 299.
...ler L., Kirk, D Ostapiak, M. (1951) *J Amer med Ass.* 146, 676
... L. (1954) *Acta paediat* 43 suppl 95
...ton, J T Scherer W F Ellwood, P M. (1954) *J Lab. clin. Med.* 43, 286
... J O H, Brunner K. T, Ellwood, P M. Syverton, J T (1954) *Bull Univ Minn Hosp* 26, 234
... Reference Laboratory (1953) *Lancet* i 85
...ren, A (1951) *Acta paediat.* 40 511
... T H (1953) *Proc. Soc exp Biol.* N Y 83 340

DENTAL CARE FOR MOTHERS AND CHILDREN

The Ministry of Health has issued a memorandum ... dental services provided by local health authorities. ... memorandum has been prepared in agreement ...h the Ministry of Education The following is a ...mary of its recommendations

EXTENT OF THE SERVICE

A satisfactory service is defined as providing for the ...amination of every expectant mother and the periodical ...amination of pre-school children followed by the ...vision of any necessary treatment Progress towards ... comprehensive service of this sort has been made ...icult by the shortage of dentists in the public dental ...rvice, but the numbers are now increasing and the ...istry suggests that authorities should review this ...rt of their maternity and child welfare service to ...re that they are making the best use of the available man power and are making such expansion as can be financially afforded

The object of treatment should be the conservation and retention of the natural teeth whenever possible and all forms of treatment should be available apart from those for which reference to hospital is necessary In a satisfactory service the number of teeth filled for expectant and nursing mothers and pre-school children should greatly exceed the number of teeth extracted. Only a few authorities have so far been able to achieve this standard

PROVIDING THE SERVICE

A local authority is not fulfilling its duty by referring mothers and children to the general dental services for any necessary advice and treatment The general dental services are of course available to the ' priority classes but some dentists are unwilling to treat small children and there is in any case no system for ensuring that these classes are put in a preferential position in relation to other patients Mothers and young children do not form a sufficiently large class to justify an entirely separate dental service and the service should therefore be coordinated with the school dental service for joint use of staff and premises Dental officers employed by the local health and education authorities should devote not less than one eleventh of their time (i e., one session of 3 hours in a 33 hour chairside week) to maternity and child welfare work This division of time should be applied even though for the present the full demands of the school and the maternity and child welfare dental services cannot be met

It is important that the dental part of the local health services should be directed by a chief dental officer who should be the principal school dental officer This officer should direct the work of the dental officers, train those who are inexperienced in the routine work of clinics, and be available for consultation It would be part of his duty to advise the medical officer of health on dental factors in health education and to train other members of the health department staff—e.g health visitors actually engaged in this work

Within the limits of expenditure available some priority should be given to the provision of further clinics (some notes on planning are given in an appendix to the memorandum) Where existing clinics are not fully used greater use can sometimes be made of them by the part time employment of general dental practitioners on a sessional basis a method which has enabled many authorities to provide in present circumstances a much more comprehensive service Evening sessions might supplement or replace morning or afternoon sessions. This system has been used with success by a few authorities, and mothers welcome the opportunity of attending for treatment at a time when the father is usually able to look after the children

So that they can spend the maximum time on operative surgery dental officers should be relieved as much as possible of other duties For this reason general anaesthetics should be administered by medical practitioners if necessary engaged for this purpose on a sessional basis. Oral hygienists can also relieve dental officers of considerable routine work in scaling and polishing teeth

Modern equipment should be provided so that as many patients as possible can be treated and so that the inevitable strain of dental work, particularly with children is minimised. X ray units should be available to serve all clinics in full time use Arrangements can be made for outside technicians to construct dentures, crowns, or inlays. If over 400 dentures or orthodontic appliances are required annually it may be advisable to consider setting up a dental laboratory and employing a dental technician.

COÖPERATION WITH OTHER SERVICES

Close coöperation with other branches of the maternity and child welfare service is essential. It is important that women should obtain dental treatment in the early stages of pregnancy and those attending antenatal clinics should be referred as a routine by the doctor or midwife to the dental officer, unless, of course, they prefer to make their own arrangements It is often an advantage to hold antenatal and dental sessions at the same time It is important to detect and treat slight defects early, and even if it is impossible to provide routine examination to all mothers, it should at least be provided for those undergoing their first pregnancy Mothers attending child-welfare clinics should be encouraged to bring their children for regular dental examination and treatment from the age of $2^1/_2$

DENTAL HEALTH EDUCATION

Education about dental health should be an essential part of the general health teaching programme As part of this programme, dental officers should, when staffing considerations permit, visit antenatal centres where there is no dental clinic, to give group talks and be available for consultation by the patients If oral hygienists are employed, an important part of their work is in dental education, and particularly in introducing young children to their first experience of dentistry Health visitors should, of course, continue to include dental health education in their advice to mothers they are in a particularly favourable position to advise mothers on the right types of food for children They should be able to recognise the early development of habits leading to deformities of the teeth and jaws such as thumb, finger, or tongue sucking Simple explanations of the cause of dental decay and the value of the filling of teeth as opposed to their premature loss should also be undertaken by them Another appendix to the memorandum gives some notes on the means of promoting preventive dentistry to guide those undertaking these duties

There are more opportunities for group teaching on dental care now that many health visitors give talks to groups of parents and others At antenatal clinics mothers are usually ready to accept advice on the need for dental treatment Home visits by the health visitor or midwife should ensure that the advice is carried out by treatment when necessary and in all cases by reference to hygiene and food value

The Ministry of Health has produced a simple single paged illustrated leaflet, suitable for the use of health visitors, which will be supplied free to authorities on request The Ministry has also reprinted the 12 panel display set, *Take Care of Your Teeth*, first sent to all local health authorities in November, 1951 Copies of this set are also obtainable free Details of these and other publicity material are given in a third appendix to the memorandum

Infectious Diseases in England and Wales

Disease	Week ended May			
	7	14	21	28*
Diphtheria	4	9	17	10
Dysentery	862	1038	1232	1385
Encephalitis				
Infective	2	4	1	2
Postinfectious	7	5	7	3
Food poisoning	155	211	160	306
Measles, excluding rubella	19,496	20,384	23,655	25,470
Meningococcal infection	29	22	27	19
Ophthalmia neonatorum	34	45	31	64
Paratyphoid fever	9	12	7	10
Pneumonia, primary or influenzal	450	441	377	423
Poliomyelitis				
Paralytic	14	11	16	12
Non paralytic	10	5	3	13
Puerperal pyrexia	274	274	209	201
Scarlet fever	575	571	620	609
Smallpox	—	—	—	—
Tuberculosis				
Respiratory	788	823	812	744
Meninges and C.N S	17	19	22	12
Other	93	108	90	85
Typhoid fever	3	2	3	1
Whooping-cough	1850	1805	1613	1455

*Not including late returns

Poliomyelitis Vaccine

The United States Public Health Service last week issued a report on the Salk poliomyelitis vaccine.[1] The breakdown of the mass vaccination programme is largely attributed to the incompatibility of the original formula with mass-production methods The experience of manufacturers showed " that the process of inactivation does not always follow the original concept " set out by Dr Salk. The Federal government lacked " adequate " procedures for determining manufacturers' performance and control because there were insufficient statistical data or experience on which they might be based The government's biological control arrangements have accordingly been reorganised, and a new Division of Biologics Standards has been created, with increased powers and facilities, to replace the Laboratory of Biologics Control, that had been in charge of the clearance of the vaccine.

During manufacture, the report states, the formalin used for inactivation often failed to reach minute particles of live virus The original safety tests were designed " primarily to demonstrate mass contamination resulting from accidents in manufacture and not small amounts of residual live virus which the process was believed to reduce to an immeasurably low and harmless level " Data obtained in a study of manufacturers' processes indicated that a single negative test (which was what the old safety standards required) was unreliable, and the minimum requirements were raised

The report gives some reasons for believing that Cutte vaccine may have contained live virus

> " The interval between injection of vaccine and first paralysis in Cutter associated cases ranged from five to twenty days The median case occurred in the ninth day and th spread was from six to fourteen days This finding parallel the frequency distribution of incubation periods in monkey infected by intramuscular injection of virus Moreover th distribution of cases following the injection of Cutter vaccin is the expected distribution in a common source outbreak o polio resulting from a single exposure to the infectious agent

Another similarity to experience with monkeys was th " high degree of correlation " between the site of injectio and the site of first paralysis

In a letter accompanying the report, Dr Leonard A Scheele, the Surgeon-General, says that " events which i the traditional course of scientific development wou have covered years were telescoped into months and, a result, both successes and failures have been magnifie In the long run, however, the nation and the worl will surely have gained from efforts to speed the avai ability of an effective immunising agent against th disease "

Parliament

The Queen's Speech

THE first session of the new Parliament was opene by the Queen on June 9 The Government have decide that the session shall continue for fifteen months, extending to the autumn of next year It is hoped to plac on the Statute Book some measures introduced but no passed in the last session, including the Road Traffi Act

The gracious Speech announced that Bills would als be introduced to safeguard the health and provide fo the safety and welfare of those employed in agricultur and forestry, to extend the period during which famil allowances were payable for children who remained a school, and to reduce the pollution of the air by smok and other causes In the light of proposals recentl agreed among the local authority associations the Government were examining the problems of local government in England and Wales with a view to introducing legislation on the subject While maintaining a high rate of house building, the Government would encourage action to secure the more rapid clearance of slums in both town and country and to relieve urban congestion Such legislation as might be found necessary uld be introduced to further these objects. Further nsideration would be given to the composition of the use of Lords.

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[1] *New York Times*, June 10, 1955

QUESTION TIME

Prohibition of Heroin

Replying to questions asking on what evidence the Ministry f Health held that an efficient substitute for heroin existed the treatment of disease and what consultations had taken ce with *medical practitioners before the decision to limit* manufacture to small quantities for scientific purposes r Iain Macleod Minister of Health, said that the British armacopœia Commission were of the view in 1950 that table alternatives existed and deleted the monograph on e drug from the 1953 edition of the *British Pharmacopœia* e Standing Medical Advisory Committee were consulted d endorsed this view As a result Mr Macleod had d the Home Secretary that there was no obstacle from standpoint to responding to the appeals of the World alth Assembly and Economic and Social Council to prohibit e manufacture of the drug Replying to Mr Somerville Hastings he added It is true that there are people who ve that for a limited range of afflictions there is no true stitute for heroin. The point is that we have to weigh is against the larger claim of playing our part in combating thing which is a very substantial social evil all over the rld, and although there may be very little evidence of diction in this country it is entirely desirable that if we n get international agreement we should prohibit the nufacture of the drug everywhere

r. Walter Elliot: Is it not a fact that the drug is really reat use in certain cases and cannot be dispensed with? ll the Minister bend his utmost efforts to ensuring that lies are made available to reputable practitioners, as has ously been done with many drugs as dangerous as this

r. Macleod: *I will gladly take that into account* I can do is to take the very best advice that is available me, which is that of my Standing Medical Advisory Com tee which includes the presidents of all the royal colleges, chairman of the council of the B.M.A the president of the ral Medical Council and many other people. Their view rely one to which we must give the greatest attention

Replying to a further question asking whether in view of the sts of the B.M.A and of the medical profession through the country against the threatened withdrawal of heroin Home Secretary would now permit the manufacture of drug in limited quantities for use by medical practitioners, subject to a ban on its export, Sir Hugh Lucas Tooth under-secretary of State for the Home Department d that the council of the B.M.A. had asked the Home tary to receive a deputation on this subject and he had ed to do so

Poliomyelitis Vaccine

Replying to a question, Mr Macleod said that a member he staff of the Medical Research Council had just returned a visit to the United States where he had been studying latest developments in regard to poliomyelitis vaccine report was at present being considered.

Dr Barnett Stross Is it not a fact that some of the results of the use of the Salk vaccine in the United were due to the fact that the virus in the vaccine was completely killed? If it is used here may we take it t the greatest care will be taken to see that no such ent occurs?—Mr Macleod: It seems probable that xplanation of the Cutter vaccine incident was that it ained live virus We in this country will be content only the very highest standards before we go ahead.

Royal Free Hospital Group Inquiry

Replying to a question Mr Macleod said that he had seen report of the subcommittee of the board of governors of Royal Free Hospital group set up to inquire into the edure for dealing with casualties at the Hampstead eral Hospital He was informed that the report had been pted by the board. They were satisfied that the pro re laid down was in itself satisfactory if properly followed he saw no reason to differ from that view What was ded was to see that it was properly followed which he sure that all concerned would now endeavour more than r do.

Medicine and the Law

A Difficult Transfusion

A RECENT inquest[1] investigated a death which followed an incompatible transfusion The patient a woman aged 54 was admitted to hospital with high intestinal obstruction valvular disease of the heart, and auricular fibrillation her blood urea was raised. Operation relieved the obstruction, and a transfusion of two bottles was ordered. Two bottles of group A blood were given to the patient, who was of group O the next day she was found to be jaundiced and her urinary output decreased but after a few days the jaundice faded and the urinary output increased again Nevertheless the blood urea remained high and the patient died 16 days after operation At necropsy the kidneys showed chronic pyelonephritis, thought to be sufficient to account for the raised blood urea, and the coroner accepted this view agreeing that the blood transfusion was not responsible for the patient's death

The interest of this case lies in the difficulties encountered by the technicians in grouping the patient's blood According to the local press report,[1] which is an unusually good one, a sample of anti A grouping serum agglutinated a number of samples of group O cells The most likely explanation of this is that the particular tube of grouping serum used was contaminated by bacteria and had become pan agglutinating—bacteriogenic hæmagglutination

Friedenreich[2] has shown that a few strains of bacteria can modify cells so that they are agglutinated by all human sera even those of group AB (the Hubener Thomsen phenomenon or T-agglutination) while Grove and Crum[3] and Davidsohn and Toharsky[4] have described the reverse phenomenon whereby a sample of serum becomes capable of agglutinating all human cells (H agglutination which has nothing to do with the rare antibody anti H)

It seems possible that in this case H agglutination may have been responsible for the technicians difficulty the regional transfusion centre found nothing wrong with the serum, but it seems possible that they received not the actual tube of serum which had been used, but another tube containing a sample of the same batch of serum which had not been contaminated by the rare bacterium which causes H agglutination Anyone unaware of this variety of bacteriogenic hæmagglutination might assume that an unused tube of the same batch would be preferable to the almost empty tube which had caused the trouble

The technicians also had difficulty in cross matching blood of group A with the recipient's serum but they ascribed this difficulty to the presence in the recipient's serum of macromolecular plasma substitutes, of which large volumes had been administered. One explanation is that they may have failed to distinguish between true agglutination (which was present) and rouleaux formation or *pseudo-agglutination* (which may also have been present) which often occurs when any blood cells are mixed with macromolecular colloids such as dextran This difficulty is well known but Marston[5] has shown that it can be overcome by using the Sheffield technique[6] in which cells and serum are incubated for about 1½ hours, after which the supernatant is removed and replaced by an equal volume of 20% bovine albumin the test being read microscopically 15 or 20 minutes

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1 *Pembroke County Guardian* June 3 19[illegible]

2 Friedenreich, V The Thomsen Hæmagglutination Phenomenon. Copenhagen 1930

3 Grove E. F., Crum M. J *J Lab clin Med* 1930 16 [illegible]

4 Davidsohn I. Toharsky B *J infect Dis* 1940 67 25 *J Immunol* 194[illegible] 43 [illegible]

5 Marston N. A. *Lancet* 1954 ii [illegible]

6 Dodge O G *J clin Path* 1953 6 102.

later, and Bowley and Dunsford[7] recommend that in such cases the anti-globulin technique should be used

Finally, having noted the difficulty in cross-matching, the two technicians decided that they must rely on the biological test in this about 50 ml blood is administered within 30 minutes, and if no reaction occurs during that time it is concluded that the blood is compatible This procedure can be refined by comparing the bilirubin levels of pre-transfusion and post transfusion samples of blood The technicians might not have realised that many incompatible transfusions do not cause any immediate reaction, and it seems that they were unaware of the Sheffield technique and its use for recipients who have received macromolecular plasma substitutes It is also probable that they were not familiar with the possibility of bacteriogenic agglutination This is not surprising, for most technicians, and many pathologists who work outside transfusion centres, would be equally unfamiliar with these possibilities Nevertheless, the situation of these technicians is one in which other technicians or junior pathologists may unhappily find themselves, and they should always have a chance of ready help from an expert Under the circumstances the technicians in this case acted wisely, within the limits of their knowledge and experience

Coitus Interruptus

The recent case of Knott *v* Knott[8] raises again the troublesome question of how far the practice of coitus interruptus should be treated as a ground for dissolving a marriage It is necessary in this connection to distinguish clearly between nullity and divorce A decree of nullity may be obtained on the inability or wilful refusal of one of the spouses to consummate the marriage It is still not clear whether insistence by the husband on coitus interruptus amounts to non consummation In the leading case of Baxter *v* Baxter,[9] in which the House of Lords decided that insistence by the wife on the use of contraceptives did not amount to non consummation, the question of coitus interruptus was specifically left undecided Later that year (1948) Mr Justice Finnimore, in the case of Grimes (otherwise Edwards) *v* Grimes,[10] granted a decree of nullity on the ground that the practice of coitus interruptus contrary to the wife's wishes amounted to non-consummation In a case decided only three days later—White (otherwise Berry) *v* White[10]—however, Mr Justice Willmer held exactly the opposite, coitus interruptus was not wilful refusal to consummate, although it might be legal cruelty if it resulted in injury to the wife's health

Mr Justice Willmer's decision was followed by Mr Justice Hodson in the case of Cackett (otherwise Trice) *v* Cackett (1950) His Lordship added that the court would be driven into an impossible position if it tried further to define what amounted to normal sexual intercourse between normally formed people, for, where a woman alleged that the man had failed to complete the sexual act, the court would have to inquire exactly at what stage emission took place or what degree of satisfaction was reached by the woman

There the position with regard to nullity remains Nevertheless, as suggested by both Mr Justice Willmer and Mr Justice Hodson in the cases just mentioned, a decree of divorce (as distinct from nullity) may be obtained on the ground of cruelty Legal cruelty has been defined as conduct of such a character as to have caused danger to life or limb or to bodily or mental health, or as to give rise to a reasonable apprehension of such danger A decree on the ground of coitus interruptus was in fact obtained in Walsham *v* Walsham (1949), in that case the husband persisted in withholding full intercourse although warned by his wife and by doctors of the probable consequences for her health which did in fact ensue

The new case of Knott *v* Knott carries the matter a stage further, since in this case a divorce was granted although the husband had not been warned by doctors of the consequences likely to result to his wife

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Mr Justice Sachs held that the husband's conduc viewed as a whole, amounted to cruelty, further, t refusal to allow the wife a child and the practice of coit interruptus in disregard of whether it injured her health not, coupled with the obvious injury to her healt amounted to cruelty even though he had not been warn by doctors of the potential results His Lordsh said

> "I am not prepared to hold that his wife's deterioration health was due to an active intent to injure his wife. I hold that in determining to continue with coitus interrupt and in refusing to let his wife have children he was reckl of the effect on his wife and that his conduct was inexcusa
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Refusal to have a Child

In another recently decided case—Forbes *v* Forbe —it was the husband who obtained the decree, it bei held that the wife's conduct in refusing to have a ch amounted to cruelty

The parties were married in 1945, both were then about Before the marriage the wife had never raised any object to having children, and she knew that the husband particularly fond of children After the marriage the w insisted on the use of contraceptives, at first the husb reluctantly agreed to use them himself, but later the w herself used them He attempted to persuade her to hav family, but she made various excuses and avoided discuss the subject as far as possible On occasions she taunted h about his desire for children By 1950, as a result of refusal to have free intercourse, their relationship had beco strained In February, 1953, the wife for the first ti definitely refused to have children and in November, 19 the parties separated By that time the husband was in bad state of health as a result of her refusal to have childre

Mr Commissioner Latey held that the wife's conduct caused injury to the husband's mental health, her cond was intentional in that she pursued it although she knew th her persistence was causing him anxiety and misery, acco ingly she had been guilty of cruelty and the husband w entitled to a decree In the course of his judgment the learn commissioner said "Quite apart from the exhortation in t solemnisation of matrimony that, first, Christian marria was ordained for the procreation of children, I cannot igno the fact that it is a natural instinct in most married men propagate the species and to bear the responsibilities an enjoy the comforts of their own children If a wife deliberate

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[7] Bowley C C, Dunsford I *Lancet* 1954, ii, 1080
[8] All England Law Reports 1955 vol. 2, p 305
[9] See *Lancet* 1948, i, 38 225
[10] *Ibid* p 883
[11] All England Law Reports, 1955 vol 2, p 311

> and consistently refuses to satisfy this natural and legitimate craving, and the deprivation reduces the husband to despair and affects his mental health, I entertain no doubt that she is guilty of cruelty

It would appear that these words are subject to the qualification that the wife's refusal must be without justification. For as Lord Justice Denning has said

> Where a man takes contraceptive measures against the will of his wife without reasonable excuse for so doing, it is easy to infer that he does it with intent to inflict misery on her but when a wife takes contraceptive measures or asks her husband to do so, her conduct can often be attributed to fear of consequences to herself without any intention of injury to him In the present case however, the wife was on record as saying that she had no fear of childbirth, and the learned commissioner had no difficulty in finding that the wife's intentional acts amounted to cruelty

Baby Sent Out Too Soon?

An infant who was discharged from hospital two days after birth died five days later from pneumonia. The inquest jury considered that the infant had been sent out too soon.[11]

> The baby was born on May 15 On May 17 the hospital told the father that his wife and the baby were to be sent home that evening They arrived home in an ambulance at 9 P.M that night when it had been snowing and it was cold, wet and [illegible] The father said in evidence that he had taken every precaution in preparing and warming the room into which his wife and baby were taken. On May 20 the baby was ill and a doctor ordered his removal to hospital where he died on May 22.
>
> The mother said in evidence that she did not think that the child had on enough clothing when it was discharged the baby seemed cold when they arrived home A staff nurse said that she wrapped the baby in blankets, and thought it was sufficiently guarded against the weather Asked if she approved of a baby going out of hospital so soon after birth, the midwife said that this was due to the bed situation; they could not do anything else It would be ideal she said, if there were bigger hospitals with better accommodation so that babies might be able to stay there for up to fourteen days.
>
> Medical evidence was given that every precaution was taken with the child and that there was nothing unusual in discharging a healthy mother and child after two days
>
> Summing up the coroner said it might strike the jury that once a decision to discharge the baby had been taken it was acted upon and had to go through. You may feel there is some lack of cohesion, coördination or supervision on the part of the hospital staff.
>
> Returning a verdict of death from natural causes, the jury added a rider that the baby was sent out of hospital too soon and that the standing order operative in the obstetric ward of the hospital regarding the discharge of mothers and such young babies be made more elastic

Newspaper's Account of an Operation

In January a newspaper published[12] an account of an operation performed by a thoracic surgeon at the Churchill Hospital Oxford The surgeon objected to this article which he had not in any way authorised He objected not only on the grounds of unwanted publicity for his name and the inaccuracies in the article but because he felt that the article might rouse unfair fears in the minds of patients who might believe that they suffered from a similar condition The Medical Defence Union accordingly instituted proceedings on his behalf against the newspaper and its issue of April 24 contained a correction of the inaccuracies and an apology to the surgeon

In England Now

A Running Commentary by Peripatetic Correspondents

INTERLUDE

The water murmurs beside me murmurs ceaselessly
While I sit still, content
My moment taken out of the current of time
The dry stones of the rocky watercourse
Pale as bleached bones, are silent as time past
While the water murmurs. Through these pared stone
Bones of the land laid bare the river flows
Deep through the narrows and spreads wide
Into a sheet of silken blue spread at my feet;
Its satin smooth blueness frayed into purple
Into the rough, purple splatches of shallows,
As I still sit stilled in the moment between
Past and present This is the moment of no momentum
Poised between memory of pleasure past
And foresight of delight
So I sit relaxed caressed by the sun and teased
By an easterly breeze looking towards a steep hillside
Where tender green of the new grass and dusty pink of
full budded trees
Please my spring sap running senses. I see with approval
The sinuous strength of the tree that thrusts
Its dark twigs above me thrusts them into the sky
With their gleaming golden spear-sharp buds
Held high, thrustingly overflowing with life And the water
murmurs
Under the cover of ceaseless plasholing rushing
Comes softly a lazy liquid gurgle
An undertone an aside of the lively river
Over the colour flickering lights of small wet boulders
Shine and signal their silent delights
While the water murmurs And I sit still

* * *

This year we sought sunshine and warmth in Spain and as by products, our search brought us one mild adventure and one diagnostic triumph

The first began on a journey by bus to San Feliu we were a willing audience to floods of abuse at the iniquitous charges of the bus from an elderly French couple and when in the evening we were taking tea on the pavement in the square they came up They were not going back in the *maudit* bus; they had hired a boat, would we share it? It had a motor oh yes! It would take only two and a half hours. Madame was the leader firm and masterful We agreed but when we saw the boat we realised that our friends were not only enterprising but intrepid. The words of the Breton sailor's prayer came into my mind: O God my boat is so small and Thy sea is so large However ashamed to jib we climbed in. The sky was greying the wind rising the boat, overloaded with six adults (two crew) faltered at the start but after rounding the point chugged cheerfully along We hugged the forbidding coast Great cliffs towered above us. Pine trees grew in clefts of the rock, almost to the water's edge We passed an occasional sandy beach at the foot of an olive grove, caves, islets, and one house perched on a height, and finally hauled up in our own bay before the hated bus could have arrived

This led to our diagnostic triumph The French couple invited us to tea A Belgian lady came in distraught her son, aged six was very ill; he had developed a cough in the plane The Spanish doctor had seen him in the morning and had given an injection of penicillin but she could not understand what he had said about the diagnosis Would the English physician tell her what was the matter with Alexander? I said doubtfully that I would try realising that the Spanish doctor had probably temporised for lack of evidence As I left the tea table *my surgical colleague* who can turn Centigrade to Fahrenheit in a trice murmured They say his temperature is 103 Luck was with me—the child would not cough there were no Koplik's spots, but as I was percussing his chest I saw a faint incipient rash and plumped for measles.

I described the course of the illness, outlined the regime, and left amid general satisfaction and relief with later and Bowley and Dunsford[7] recommend that in such cases the anti globulin technique should be used

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[11] Manchester Guardian June 7 1955. Birmingham Post June [illegible] 1955

[12] The People, Jan. 9 1955.

Finally, having noted the difficulty in cross matching, the two technicians decided that they must rely on the biological test in this about 50 ml blood is administered within 30 minutes, and if no reaction occurs during that time it is concluded that the blood is compatible This procedure can be refined by comparing the bilirubin levels of pre transfusion and post transfusion samples of blood The technicians might not have realised that many incompatible transfusions do not cause any immediate reaction, and it seems that they were unaware of the Sheffield technique and its use for recipients who have received macromolecular plasma substitutes It is also probable that they were not familiar with the possibility of bacteriogenic agglutination This is not surprising, for most technicians, and many pathologists who work outside transfusion centres, would be equally unfamiliar with these possibilities Nevertheless the situation of these technicians is one in which other technicians or junior pathologists may unhappily find themselves, and they should always have a chance of ready help from an expert Under the circumstances the technicians in this case acted wisely, within the limits of their knowledge and experience

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Mr Justice Sachs held that the husband's conduct viewed as a whole, amounted to cruelty, further, the refusal to allow the wife a child and the practice of coitus interruptus in disregard of whether it injured her health or not, coupled with the obvious injury to her health amounted to cruelty even though he had not been warned by doctors of the potential results His Lordship said

> "I am not prepared to hold that his wife's deterioration in health was due to an active intent to injure his wife I do hold that in determining to continue with coitus interruptus and in refusing to let his wife have children he was reckless of the effect on his wife and that his conduct was inexcusable
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In another recently decided case—Forbes *v* Forbes[11]—it was the husband who obtained the decree, it being held that the wife's conduct in refusing to have a child amounted to cruelty

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Mr Commissioner Latey held that the wife's conduct had caused injury to the husband's mental health, her conduct was intentional in that she pursued it although she knew that her persistence was causing him anxiety and misery, accordingly she had been guilty of cruelty and the husband was entitled to a decree In the course of his judgment the learned commissioner said "Quite apart from the exhortation in the solemnisation of matrimony that, first, Christian marriage was ordained for the procreation of children, I cannot ignore the fact that it is a natural instinct in most married men to propagate the species and to bear the responsibilities and enjoy the comforts of their own children If a wife deliberately

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[7] Bowley C C Dunsford I *Lancet* 1954 ii 1060

[8] All England Law Reports 1955 vol 2 p 305

[9] See *Lancet* 1948 i 38 225

[10] *Ibid* p 883

[11] All England Law Reports, 1955 vol 2, p 311

and consistently refuses to satisfy this natural and legitimate [illegible] and the deprivation reduces the husband to despair and affects his mental health, I entertain no doubt that she is guilty of cruelty

It would appear that these words are subject to the qualification that the wife's refusal must be without justification. For as Lord Justice Denning has said "Where a man takes contraceptive measures against the will of his wife without reasonable excuse for so doing it is easy to infer that he does it with intent to inflict misery on her, but when a wife takes contraceptive measures or asks her husband *to do so* her conduct can often be attributed to fear of consequences to herself without any intention of injury to him." In the present case however the wife was on record as saying that she had no fear of childbirth, and the learned commissioner had no difficulty in finding that the wife's intentional acts amounted to cruelty

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Medical evidence was given that every precaution was taken with the child and that there was nothing unusual in discharging a healthy mother and child after two days

Summing up the coroner said *it might strike the jury* that once a decision to discharge the baby had been taken it was a [illegible] and had to go through You may feel there is some lack of cohesion, coordination, or supervision on the part of the hospital staff.

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[12] *Manchester Guardian* June 7 1955. *Birmingham Post* June 8 1955

[13] *The People* Jan. 9 1955

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Into the rough purple splatches of shallows,
As I still sit stilled in the moment between
Past and present This is the moment of no momentum
Poised between memory of pleasure past
And foresight of delight
So I sit relaxed caressed by the sun and teased
By an easterly breeze looking towards a steep hillside
Where tender green of the new grass and dusty pink of full budded trees
Please my spring sap running senses I see with approval
The sinuous strength of the tree that thrusts
Its dark twigs above me thrusts them into the sky
With their gleaming golden spear sharp buds
Held high, thrustingly overflowing with life And the water murmurs
Under the cover of ceaseless plasheling rushing
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Finally, having noted the difficulty in cross matching, the two technicians decided that they must rely on the biological test in this about 50 ml blood is administered within 30 minutes, and if no reaction occurs during that time it is concluded that the blood is compatible This procedure can be refined by comparing the bilirubin levels of pre transfusion and post transfusion samples of blood The technicians might not have realised that many incompatible transfusions do not cause any immediate reaction , and it seems that they were unaware of the Sheffield technique and its use for recipients who have received macromolecular plasma substitutes It is also probable that they were not familiar with the possibility of bacteriogenic agglutination This is not surprising , for most technicians, and many pathologists who work outside transfusion centres, would be equally unfamiliar with these possibilities Nevertheless, the situation of these technicians is one in which other technicians or junior pathologists may unhappily find themselves, and they should always have a chance of ready help from an expert Under the circumstances the technicians in this case acted wisely, within the limits of their knowledge and experience

Coitus Interruptus

The recent case of Knott *v* Knott[8] raises again the troublesome question of how far the practice of coitus interruptus should be treated as a ground for dissolving a marriage It is necessary in this connection to distinguish clearly between nullity and divorce A decree of nullity may be obtained on the inability or wilful refusal of one of the spouses to consummate the marriage It is still not clear whether insistence by the husband on coitus interruptus amounts to non consummation In the leading case of Baxter *v* Baxter,[9] in which the House of Lords decided that insistence by the wife on the use of contraceptives did not amount to non consummation, the question of coitus interruptus was specifically left undecided Later that year (1948) Mr Justice Finnimore, in the case of Grimes (otherwise Edwards) *v* Grimes,[10] granted a decree of nullity on the ground that the practice of coitus interruptus contrary to the wife's wishes amounted to non consummation In a case decided only three days later—White (otherwise Berry) *v* White[10]—however, Mr Justice Willmer held exactly the opposite , coitus interruptus was not wilful refusal to consummate, although it might be legal cruelty if it resulted in injury to the wife's health

Mr Justice Willmer's decision was followed by Mr Justice Hodson in the case of Cackett (otherwise Trice) *v* Cackett (1950) His Lordship added that the court would be driven into an impossible position if it tried further to define what amounted to normal sexual intercourse between normally formed people , for, where a woman alleged that the man had failed to complete the sexual act, the court would have to inquire exactly at what stage emission took place or what degree of satisfaction was reached by the woman

There the position with regard to nullity remains Nevertheless, as suggested by both Mr Justice Willmer and Mr Justice Hodson in the cases just mentioned, a decree of divorce (as distinct from nullity) may be obtained on the ground of cruelty Legal cruelty has been defined as conduct of such a character as to have caused danger to life or limb or to bodily or mental health, or as to give rise to a reasonable apprehension of such danger A decree on the ground of coitus interruptus was in fact obtained in Walsham *v* Walsham (1949) , in that case the husband persisted in withholding full intercourse although warned by his wife and by doctors of the probable consequences for her health which did in fact ensue

The new case of Knott *v* Knott carries the matter a stage further, since in this case a divorce was granted although the husband had not been warned by doctors of the consequences likely to result to his wife

The husband and wife were married in 1942 when she was not quite 17 and he was 22 She was of a sensitive disposition, more liable than most people to be affected by events, and she greatly wanted to have a child The man was insensitive to the point of recklessness and did not want children After marriage they had no home of their own but lived with her parents , there were long separations due to the war, from which he returned in 1945 During the ensuing years the husband often acted in an aggressive manner towards the wife and there were quarrels between them In 1946 the wife was ill with tuberculosis In 1953 the husband left the wife, who refused to follow him and continued to live in her parents' home. Throughout substantially the whole period of the marriage he had refused full sexual intercourse and had practised coitus interruptus against her will He had not received advice from any doctor that the continuance of this practice would injure her health

Mr Justice Sachs held that the husband's conduct, viewed as a whole, amounted to cruelty , further, the refusal to allow the wife a child and the practice of coitus interruptus in disregard of whether it injured her health or not, coupled with the obvious injury to her health, amounted to cruelty even though he had not been warned by doctors of the potential results His Lordship said

> " I am not prepared to hold that his wife's deterioration in health was due to an active intent to injure his wife, *I do* hold that in determining to continue with coitus interruptus and in refusing to let his wife have children he was reckless of the effect on his wife and that his conduct was inexcusable
>
> I would hold that for a man deliberately and without good reason permanently to deny a wife who has a normally developed maternal instinct a fair opportunity to have even a single child is of itself cruelty when injury to herself results and when the husband adopts a course which preserves to himself a measure of sexual enjoyment "

Refusal to have a Child

In another recently decided case—Forbes *v* Forbes[11]—it was the husband who obtained the decree, it being held that the wife's conduct in refusing to have a child amounted to cruelty

The parties were married in 1945 , both were then about 26 Before the marriage the wife had never raised any objection to having children, and she knew that the husband was particularly fond of children After the marriage the wife insisted on the use of contraceptives , at first the husband reluctantly agreed to use them himself, but later the wife herself used them He attempted to persuade her to have a family, but she made various excuses and avoided discussing the subject as far as possible On occasions she taunted him about his desire for children By 1950, as a result of her refusal to have free intercourse, their relationship had become strained In February, 1953, the wife for the first time definitely refused to have children and in November, 1953, the parties separated By that time the husband was in a bad state of health as a result of her refusal to have children

Mr Commissioner Latey held that the wife's conduct had caused injury to the husband s mental health , her conduct was intentional in that she pursued it although she knew that her persistence was causing him anxiety and misery , accordingly she had been guilty of cruelty and the husband was entitled to a decree In the course of his judgment the learned commissioner said " Quite apart from the exhortation in the solemnisation of matrimony that, first, Christian marriage was ordained for the procreation of children, I cannot ignore the fact that it is a natural instinct in most married men to propagate the species and to bear the responsibilities and enjoy the comforts of their own children If a wife deliberately and consistently refuses to satisfy this natural and legitimate craving and the deprivation reduces the husband to despair and affects his mental health I entertain no doubt that she is guilty of cruelty

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[7] Bowley C C Dunsford I *Lancet* 1954, ii 1050
[8] All England Law Reports 1955, vol 2 p 305
[9] See *Lancet* 1948 i, 38 225
[10] *Ibid* p 883
[11] All England Law Reports, 1955 vol 2, p 311

It would appear that these words are subject to the qualification that the wife s refusal must be without justification For as Lord Justice Denning has said

Where a man takes contraceptive measures against the will of his wife without reasonable excuse for so doing it is easy to infer that he does it with intent to inflict misery on her, but when a wife takes contraceptive measures or asks her husband to do so her conduct can often be attributed to fear of consequences to herself without any intention of injury to him In the present case however the wife was on record as saying that she had no fear of childbirth and the learned commissioner had no difficulty in finding that the wife s intentional acts amounted to cruelty

Baby Sent Out Too Soon?

An infant who was discharged from hospital two days after birth died five days later from pneumonia The inquest jury considered that the infant had been sent out too soon[12]

The baby was born on May 15 On May 17 the hospital told the father that his wife and the baby were to be sent home that evening They arrived home in an ambulance at 9 P.M on a night when it had been snowing and it was cold, wet, and windy The father said in evidence that he had taken every precaution in preparing and warming the room into which his wife and baby were taken. On May 20 the baby was ill and a doctor ordered his removal to hospital where he died on May 22.

The mother said in evidence that she did not think that the child had on enough clothing when it was discharged the baby seemed cold when they arrived home A staff midwife said that she wrapped the baby in blankets, and thought it was sufficiently guarded against the weather Asked if she approved of a baby *going out of hospital so soon* after birth, the midwife said that this was due to the bed situation they could not do anything else. It would be ideal she said if there were bigger hospitals with better accommodation so that babies might be able to stay there for up to fourteen days.

Medical evidence was given that every precaution was taken with the child and that there was nothing unusual in discharging a healthy mother and child after two days.

Summing up the coroner said it might strike the jury that once a decision to discharge the baby had been taken it was cast-iron and had to go through. You may feel there is some lack of cohesion, coördination or supervision on the part of the hospital staff.

Returning a verdict of death from natural causes, the jury added a rider that the baby was sent out of hospital too soon and that the standing order operative in the obstetric ward of the hospital regarding the discharge of mothers and such young babies be made more elastic

Newspaper's Account of an Operation

In January a newspaper published[13] an account of an operation performed by a thoracic surgeon at the Churchill Hospital Oxford The surgeon objected to this article which he had not in any way authorised He objected not only on the grounds of unwanted publicity for his name and the inaccuracies in the article, but because he felt that the article might rouse unfair hopes in the minds of patients who might believe that they suffered from a similar condition The Medical Defence Union accordingly instituted proceedings on his behalf against the newspaper and its issue of April 24 contained a correction of the inaccuracies and an apology to the surgeon.

In England Now

A Running Commentary by Peripatetic Correspondents

INTERLUDE

The water murmurs beside me murmurs ceaselessly
While I sit still, content
My moment taken out of the current of time
The dry stones of the rocky watercourse
Pale as bleached bones are silent as time past
While the water murmurs. Through these pared stone
Bones of the land laid bare the river flows
Deep through the narrows and spreads wide
Into a sheet of silken blue spread at my feet
Its satin smooth blueness frayed into purple
Into the rough purple splatches of shallows,
As I still sit stilled in the moment between
Past and present This is the moment of no momentum
Poised between memory of pleasure past
And foresight of delight.
So I sit relaxed caressed by the sun and teased
By an easterly breeze looking towards a steep hillside
Where tender green of the new grass and dusty pink of
full budded trees
Please my spring sap running senses. I see with approval
The sinuous strength of the tree that thrusts
Its dark twigs above me thrusts them into the sky
With their gleaming golden spear-sharp buds
Held high thrustingly overflowing with life And the water
murmurs
Under the cover of ceaseless plasheling rushing
Comes softly a lazy liquid gurgle
An undertone an aside of the lively river
Over the colour flickering lights of small wet boulders
Shine and signal their silent delights
While the water murmurs. And I sit still

* * *

This year we sought sunshine and warmth in Spain and, as by products our search brought us one mild adventure and one diagnostic triumph

The first began on a journey by bus to San Feliu: we were a willing audience to floods of abuse at the iniquitous charges of the bus from an elderly French couple and when in the evening we were taking tea on the pavement in the square they came up They were not going back in the *maudit* bus they had hired a boat would we share it? It had a motor oh yes! It would take only two and a half hours. Madame was the leader firm and masterful We agreed but when we saw the boat we realised that our friends were not only enterprising but intrepid The words of the Breton sailor's prayer came into my mind: O God my boat is so small and Thy sea is so large. However ashamed to jib we climbed in The sky was greying the wind rising the boat, overloaded with six adults (two crew) faltered at the start but after rounding the point chugged cheerfully along We hugged the forbidding coast Great cliffs towered above us Pine trees grew in clefts of the rock, almost to the water s edge We passed an occasional sandy beach at the foot of an olive grove caves, islets and one house perched on a height and finally hauled up in our own bay before the hated bus could have arrived

This led to our diagnostic triumph The French couple invited us to tea A Belgian lady came in distraught her son aged six, was very ill; he had developed a cough in the plane The Spanish doctor had seen him in the morning and had given an injection of penicillin but she could not understand what he had said about the diagnosis. Would the English physician tell her what was the matter with Alexander? I said doubtfully that I would try realising that the Spanish doctor had probably temporised for lack of evidence As I left the tea table my surgical colleague who can turn Centigrade to Fahrenheit in a trice murmured They say his temperature is 103 Luck was with me—the child would not cough there were no Koplik s spots but as I was percussing his chest I saw a faint incipient rash and plumped for measles.

I described the course of the illness outlined the routine, and left amid general satisfaction and relief with the words "he will begin to be better in three days" My own relief was quite as intense when I learnt that the disease had played the game

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[12] Manchester Guardian June 7 10 ; Birmingham Post June 4 1955

[13] The People Jan. 9 1955

* * *

My morning paper comes from a northern city and is renowned for its clarity of thought and grace of expression It even found its way regularly to London, to my smug satisfaction, when the London papers failed recently for a period to appear

In a recent issue the last sentence in an article on Labour's likely investigations into its failure at the election read "The post-mortem will undoubtedly be long, thorough, and not painless" Although I am not in the way of writing to editors I could not resist dropping a note quoting this, and, with my tongue in my cheek and a large exclamation mark at the end, saying that the idea that a post-mortem could be painful might deter many people and their relatives from allowing autopsies I am not surprised that my letter was not published but a courteous assistant editor, a few days later, replied thanking me and pointing out that a post-mortem could cause pain to relatives

Wondering whether it was worth arguing with this undoubtedly highly educated party as to what was the difference between pain and mental distress, I happened to take up the issue of the paper for that day and there, quoting Mr Bevan from *Tribune* was the sentence "It is, perhaps, inevitable for a post-mortem to be held on Labour's defeat, but those who hasten to take part in it should keep in mind that it is a living body they are about to examine"

I do not think I will bother with journalists' or politicians' ideas of post-mortems any more

* * *

A somatotype of my acquaintance—a bit of an ectopene, actually—whom I met on the Heath while exercising our respective dogs, confessed to me that he had had great difficulty in remembering the physical and mental traits associated with the three standard types until he had related them to the canine world "whose characteristics," he added, "are so much better known to the average Englishman than those of his human associates Take a pug," he said, "a typical endomorph! His podgy physique, love of good food—stomach before sex is his motto—and insistence on postural ease and comfort would rate him as a 711 The peke, with his bland and tolerant outlook and love of polite ceremony—I quote the literature—is another endomorph, though I admit that, confronted with a rabbit, he becomes pretty mesomorphic The aggressiveness, the love of exercise, of action and even of combat, and the vehemence of expression (*Will* you stop barking, Spot!) mark the terriers as the supreme mesomorphs And the greyhounds, collies, and red setters, with their linear outlines and speedy mental and physical reactions, fall naturally into the ectomorphs" "Thank you," said I, "for these hints As a mesomorphic-ectomorphic-endomorph may I suggest that we now drop in to The Spaniards and have one?" "Willingly," he replied, "but meanwhile do not let us forget that there is an earlier and more elegant description of the type you have just mentioned, I mean, *l'homme moyen sensuel*"

* * *

News from School —"I gained six pounds (weight unfortunately) in the holidays Last night I attempted to ride a horse tethered in the Park The horse however did not want to be ridden so after giving it about 10*s* worth of sweets it kicked up various legs And this somewhat dismayed me, so I continued on my way to the dreadful Entertainment This was a Dutchman (Deutch) who could multiply 12 figure numbers together in his head In the end the headmaster asked him to answer any questions that 'the boys may put' He said No, I don t want to answer any questions, please may I go now?' The headmaster took no notice as the Dutchman had not a very good accent, so the headmaster repeated his request The Dutchman said 'Thees vaas not on ze programme,' however, he wrote a lot of figures on the blackboard and asked us if we understood We said that [illegible] and he rushed out"

Letters to the Editor

CHILDREN'S TEETH

SIR,—May I appeal to all medical practitioners, and through them to nurses and medical auxiliaries who have contact with children (and mothers), to emphasise the necessity of regular dental inspection and early treatment? The increasing number of cases where teeth of the permanent dentition are lost prematurely is appalling. We are creating daily more orthodontic and dental problems than our undermanned dental profession can hope to deal with One wonders whether our educational system is lacking Should not more attention be paid to teaching oral hygiene in the schools, since in many homes the parents are too ignorant or too apathetic to take an interest in their children?

When many of the present day school children become parents the whole sorry story will be repeated Last year the British Dental Association presented a memorandum on child dental health to the Ministries of Health and Education, and it is to be deplored that the medical press have not seen fit to publish a résumé of this important document

Prevention is the important aspect of the problem because owing to an increasing shortage of dentists we cannot give adequate treatment to all classes The priority classes should, of course, have preference, but, pending national arrangements to secure adequate treatment of children, let us try to attack the problem by attention to diet and hygiene

Selly Oak Hospital,
Birmingham
EDWARD LINE

*** The Ministry of Health has just issued a memorandum (prepared in agreement with the Ministry o Education), on the dental care of mothers and children A summary appears on p 1269 —ED L

PSYCHOSOMATIC DISEASES IN UNDERDEVELOPED AREAS

SIR,—Osler's remark that "As clinicians we observ the experiments of Nature," would seem to apply on grand scale to Professor Davidson's observations (April 2 on the incidence of those diseases which are commonl called "psychosomatic" The evidence which he present in his letter is of importance to all concerned with th problem of the ætiology of rheumatoid arthritis As ou findings here are somewhat similar to his own, they ma be of interest to others working in the same field, as wel as to politicians and health authorities engaged in th development of "underdeveloped areas"

In the Queen Elizabeth Hospital for Rheumatic Diseases, which is situated in a district with a large Maor population, we see very few Maori patients with rheumatoid arthritis In the past year I have seen only 3 and it may be significant that all of them were eithe married to Pakehas, or had a history of previous neisserian infection, or both The rarity of rheumatoi arthritis, and of other diseases commonly called "psychosomatic," amongst Maoris (in the areas away from th two largest cities in the North Island of New Zealand, is confirmed by several general practitioners with whom I have spoken, so that I am not inclined to think that my experience, based on hospital cases, is unrepresentative

Hitherto it has not been easy to decide whether to attribute this great difference in incidence to genetic or to environmental factors Now, in the light of Professor Davidson's observations, it would appear that environmental factors would be a more likely explanation than a genetically determined racial immunity

He raises the question of the relative importance of metabolic and emotional factors in the ætiology of these disorder Here one is on very uncertain ground, but emotional factors would appear to be frequently operative in initiating the abnormal metabolic processes involved Our experience of rheumatoid arthritis in patients here accords very well with that of Professor Hartfall[1] who found associated emotional disturbance in 68% of his series According to Halliday[2] one of the hallmarks of diseases of emotional origin is a tendency for the peak incidence to shift to an earlier age group and for the severity to increase, with continual failure of adaptation to environmental pressure The observations of the distinguished physicians mentioned in Professor Davidson s letter could therefore be interpreted as supporting an emotional ætiology

The Maori population is not as yet reacting with the same type of emotional disturbance possibly because their culture is less competitive and because they are less exposed to "social isolation, especially when compared with Pakeha immigrants This does not mean that the Maoris are immune from emotional disturbance but only that it takes different forms The present risk is that, in freeing themselves from the danger of psychosomatic death following infringement of a taboo they may become more liable to peptic ulcers and to rheumatoid arthritis

As it has taken less than forty years for this change to occur in the United States of America it is of some importance to public-health administrators to know how to prevent a parallel change elsewhere without sacrificing a high material living standard In this respect it has been shown by LeCorbusier that it is not by any means necessary for a materially advanced culture either to cut itself off from the basic rhythms of nature, or to split itself up into a disintegrated state of individual social isolation, as is the present trend These last remarks apply to the development of developed areas, but in dealing with undeveloped ' areas they might do worse than consult the UNESCO handbook *Cultural Patterns and Technical Change*[3] Consultation with a cultural anthropologist before initiating any major changes such as housing schemes in new factory areas could prevent major social disintegration even if the Corbusian dream remains long unrealised.

Queen Elizabeth Hospital
Rotorua New Zealand

B S ROSE

HYPERSENSITIVITY ANGIITIS

SIR,—In their article of June 4 Dr Edge and his colleagues describe a case of polyarteritis which followed a typical and mainly progressive course, starting with lesions of the respiratory tract and ending with glomerular involvement and renal failure The patient was treated successively with penicillin streptomycin isoniazid and cortisone. They suggest that hypersensitivity to penicillin caused the disease and that hypersensitivity to the other drugs aggravated it

The theory that drug hypersensitivity can cause or aggravate polyarteritis is, except in the case of thiouracil founded largely on observations of this sort. Such evidence is unconvincing for two reasons Firstly it is possible that the initial condition for which the drug was given may have been polyarteritis and not a simple infection Secondly even in the absence of any treatment the disease is liable to repeated exacerbations it is therefore to be expected that the giving of drugs may often by pure coincidence be followed by deterioration

In the present case, the authors date the onset of polyarteritis from the appearance of a skin rash and lung lesions, regarding the ' otitis media ' which preceded these as a simple infection. But experience strongly suggests that the otitis media in this case was due to specific granulomatous lesions and was thus a part of the polyarteritic illness. This is a not uncommon presentation in cases of polyarteritis with lung involvement. If this view is correct then clearly the penicillin treatment of the ear condition did not cause the polyarteritis During the *subsequent course* of the disease the association between drug treatments and exacerbations of polyarteritis was no more than could be readily explained by chance To infer a causal relation from such evidence is only to confuse our understanding of the disease, especially when the postulated causes are multiple

Dr Edge and his colleagues *go on to argue* that corticotrophin should be used rather than cortisone in the treatment of the disease. Their opinion is based firstly on reports of polyarteritis occurring in cases of rheumatoid arthritis treated with cortisone and secondly on the observation of Rich and his co workers of a peculiar form of glomerulitis in sensitised rabbits treated with cortisone. The first observation must be interpreted with caution since rheumatoid arthritis quite commonly precedes polyarteritis even in the absence of cortisone therapy and in the second instance it *is unjustifiable* to identify the experimental lesions with human polyarteritis Cortisone has been used extensively in the treatment of polyarteritis, and I have personally had access (mostly through the Medical Research Council) to over 40 such cases without finding any evidence of its causing either hypersensitivity or renal damage. In adequate dosage (which may mean 500 mg daily or even more) it prevents the appearance of new lesions in nearly all cases In these circumstances it seems reasonable to continue to use this form of treatment –

St Mary's Hospital
London W 2

GEOFFREY ROSE.

LUNG CANCER IN ASBESTOSIS

SIR,—In your annotation of June 4 the final sentence poses an important question The dust diseases generally act on the connective tissues and there is no satisfactory explanation of why the asbestos fibres should affect the epithelium as well '

The answer to this problem may well be found in a consideration of the histology of human asbestosis. The essential pathological lesion in asbestosis is a fibrosis around the respiratory bronchiole with thickening of alveolar walls and included asbestosis bodies Asbestosis bodies are found in the respiratory bronchioles and alveoli as well as interstitially There is evidence to show that asbestosis is initiated by the inhalation of fibres whose length is between 20 and 50 microns[1] The flexibility of such a fibre enables it to reach the respiratory bronchiole but its size renders removal by phagocytes difficult or impossible Small asbestos particles and fibres under 5 microns can be engulfed by phagocytes and removed by lymphatic channels or dissolved in tissue fluids. Many long fibres penetrate the bronchiolar and alveolar walls, while others go through their characteristic changes in these epithelially lined spaces. As the pathological changes become more advanced there is much thickening of alveolar walls with imprisoned clumps ' of asbestosis bodies

Gloyne stated[2] When the diffuse fibrosis has reached an advanced stage all alveoli in the area may be compressed out of recognition. Here surely we have an environment which allows chronic irritation by a fibrous mineral to epithelium This irritation reacts on the epithelium in circumstances of increasing abnormality The asbestosis body moreover is undergoing slow changes well described by Gloyne[2] which ultimately result in its disintegration With the increasing fibrotic condition of the involved areas there is a possibility of a chemical effect on the tissues from the solution of the bodies in these abnormal conditions

In view of these facts there would seem to be no lack of opportunity for the asbestos fibre and bodies form from fibres or chemical material produced by the disintegration of bodies, to affect epithelial structures in the lungs

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[1] Hartfall, S J Brit J phys Med 1955 18 1[illegible]
[2] Halliday J L Psychosocial Medicine London 1910
[3] Cultural Patterns and Technical Change Edited by Margaret Mead. UNESCO 1954

[1] Vorwald A J Durkin T M, Pratt P C [illegible] 19 1 3 1
[2] Gloyne S R [illegible] and Asbestosis [illegible] 231

Rochdale J F KNOX

CYCLICAL VOMITING

SIR,—The letter of Dr Millichap in your issue of Feb 19, commenting on Dr Wallis's paper (Jan 8), and Dr Wallis's subsequent letter (Feb 26), gives the impression that most or all cases of cyclical vomiting are epileptic in origin Some may be, but, lest all children who have the disorder be stigmatised as having epilepsy, accurate diagnosis is important It should be pointed out that in certain cases, at least, no evidence of epilepsy is present The disorder may recur in uniform episodes with remarkably regular periodicity for years, which is not characteristic of epilepsy In some patients, cyclical vomiting persists or recurs in adult life in a different recurrent form Such patients I regarded as having one of the bizarre forms of periodic disease of unknown cause[1]

University of California
University of Indonesia
Project in Medical Education
Djakarta Indonesia

HOBART A REIMANN

PROTEINURIA

SIR,—The work of Greiner and Henry,[2] to which you referred on June 4, may throw light not only on the mechanism of postural proteinuria but also on that of proteinuria in heart failure

On the basis of their own investigation and that of Farber et al,[3] Greiner and Henry criticise the view[4] that postural proteinuria is due to increased renal venous pressure causing passive congestion of the kidneys They refer to the work of Pappenheimer[5] and suggest, with regard to the intrarenal mechanism, that postural proteinuria is due to slowing of the glomerular blood flow, resulting in an abnormal glomerular filtration of albumin, and to decreased tubular resorption of the protein in the glomerular filtrate They attribute both factors to renal arterial vasoconstriction

It is at present generally held that proteinuria in congestive heart-failure is due to passive venous congestion of the kidneys resulting from failure of the right ventricle This view is based on the "back-pressure" concept of heart failure I have presented evidence, however, showing that proteinuria may result from left ventricular failure, and indicating that proteinuria in biventricular congestive failure is due to the failure of the left ventricle[6] My findings appear to support the "forward-failure" concept of heart failure, and perhaps signify that the mechanism of proteinuria is similar to that suggested by Greiner and Henry for postural proteinuria

This possibility is strengthened by the occurrence, in postural proteinuria and in congestive heart-failure with a low or normal cardiac output, of certain other features in common, in addition to the protein in the urine These are a decreased circulation rate, stasis of blood in the legs, and oliguria On the other hand, in congestive heart-failure with a high cardiac output, in which the circulation rate and rate of blood flow in the legs may be normal or increased, proteinuria[7,8] and oliguria[9] may be absent

London W 1 J J SEGALL

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1 *Arch intern Med* 1953 92 494, *Medicine, Baltimore* 1951, 30 219
2 Greiner T Henry J P *J Amer med Ass* 1955, 157 1373
3 Farber S J Becker W H, Eichna, L W *J clin Invest* 1953 32 1145
4 Bull G M *Clin Sci* 1948, 7, 77
5 Pappenheimer J R *Physiol Rev* 1953, 33, 387
6 Segall J J *Med Pr* 1954 12 273
7 Segall J J *Med World Lond* 1952 7 176
8 ll J J *Lancet* 1953 1, 524
rr A M. Heart Failure London, 1940

THE ACTION OF CHLORPROMAZINE

SIR,—I am glad that Professor Samson Wright (April 2) has given his opinion a priori on the "phenomena of Reilly" this letter showed how far removed the experimental facts are from traditional physiology, and therefore justified the importance we have for a considerable time attached to this study His letter also showed the need to add a few complementary details, the development of which can be found in the works referred to by Dr Buxton Hopkin (March 19)

I have suggested that the expression "phenomena of Reilly" should include all non-specific disturbances attributable to aggression of very different kinds (chemical, physical, bacterial, &c), and I proposed this as a mark of respect to the chief of the school who, following others, undertook this study and who has done most to define these phenomena more precisely, to show their importance in the pathogenesis of many illnesses, and to indicate the primary rôle of the visceral nervous system in their development[1]

Non specific phenomena have been the subject of a great many researches in the past sixty years At the beginning of this century the non specific reaction of the adrenal cortex and medulla had been particularly implicated[2] The part played by the nervous system in these disturbances assumed more importance following the work of such people as Ricker in Germany, and Speransky in Russia But it was Reilly and his collaborators who supplied most details in this connection, and who definitely showed the importance of the irritation of visceral nerves

The experimental facts revealed by the Reilly school have been confirmed subsequently by so many authors that there is no longer any point in confirming them, as Professor Samson Wright suggests Any research-worker can easily reproduce them in any laboratory It would certainly be useful, as Dr Hopkin suggests, to study in Anglo Saxon countries these phenomena whose recognition represents in our eyes one of the most important discoveries of biology and medicine in the past thirty years, but which still remain very mysterious from several points of view One can only quote in this respect the works of Selye The "reaction of alarm," subsequently described by Selye, is in fact the same as the phenomena described earlier by French workers But his pathogenic concept is directly connected with the old suprarenal theory held in France at the beginning of this century[2] The insufficiency of this theory now seems to us to have been well established and I have indicated elsewhere, on the basis of precise and confirmed experimental facts, that the "general syndrome of adaption" does not exist[3]

Professor Samson Wright is justified when he says that the experimental facts revealed by Reilly and his collaborators are unexpected to a physiologist I have already insisted on the importance of this fact and I must emphasise that I proposed the expression "*phenomena* of Reilly" because in my opinion there are two separate groups of fundamentally different phenomena, which it has for long been difficult to differentiate since they often appear to be confused

(*a*) Adaptive reactions, normal and pathological, which are in the category studied by traditional physiology

(*b*) Cellular disturbances, more or less prolonged and whose histological and clinical sequelæ may only appear after a very long latent period These may escape the laws of classic physiology and that is why I have distinguished them by the name "neuxenic phenomena" from phenomena responding to the classic laws from which they have not yet been isolated. They often appear a long time after the aggression which caused them and they can be noticed normally only when the laboratory animals are observed for a long period and are operated on under very stringent aseptic conditions (especially as they habitually show a fall in general immunity) Neither of these conditions is generally observed in the common run of physiological research Furthermore, neuxenic phenomena respond to special biological laws, in which the laws of probability play a notable part, having an importance

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1 Decourt, P Phénomènes de Reilly et syndrome général d adaptation de Selye Paris 1951
2 Decourt P *Pr méd* 1952, 60 663
3 Decourt P *Ibid* p 1028

comparable with the quantitative laws which represent one of the most important discoveries of the atomic physicists

It is these neuxenic phenomena—which comprise only a part of the phenomena of Reilly but which play an important rôle in pathology—that have truly baffled on the one hand all attempts at an explanation of the phenomena of Reilly in terms of conventional physiological thought[4] and on the other hand the numerous efforts made over the last twenty years to prevent them.

The researches of the school of Reilly have above all been devoted to works of 'pure science but they have nevertheless had happy consequences in applied science. In effect it was the studies on the pathogenesis of the phenomena of Reilly and the efforts to prevent them which beginning in 1935 led to the discovery of antihistamine therapy in 1941 and to narcobiotic therapy in 1951 The results obtained were indeed negative with the antihistamines and that is why when I published the first results of antihistamine therapy in man in 1942 I did not speak on that occasion of phenomena of Reilly which had been the starting point of our research[5] Reilly has himself emphasised that it was in 1952 after seventeen years' research that it was at last possible to exert an effect on the phenomena, thanks to chlorpromazine But these results are still very inadequate I fear indeed that from their very nature no therapeutic procedures can ever completely prevent the neuxenic phenomena which represent the most serious disorder of the phenomena of Reilly We can however hope to improve the methods of preventing them

Paris. PHILIPPE DECOURT

CHLORPROMAZINE AND EPILEPSY

SIR,—The occurrence of convulsions during treatment with chlorpromazine has been reported recently in two papers in your columns.[6] [7]

A few months ago a seizure was observed in an epileptic patient attending an outpatient clinic of this hospital who had been free from fits for 2 years and had been given chlorpromazine by mouth for a few weeks. The convulsion occurred during photic stimulation in the course of a routine E.E.G examination. This observation suggested an investigation into the effect of chlorpromazine on the E.E.G of epileptics

So far fourteen epileptic patients have been examined After a routine E.E.G including overbreathing and photic stimulation, an intravenous injection of chlorpromazine is given (1 ml. [25 mg] diluted to 10 ml with normal saline) The amounts vary from 7 mg for a child to 25 mg for an adult The injection is given slowly 1–2 ml. (5–5 mg) every 1–2 minutes.

In seven cases no specific changes have been seen These patients had never shown grossly abnormal inter-seizure recordings. In the other seven cases the previously observed abnormal features increased but no new abnormal phenomena were seen. Thus in a child of 10 with clinical petit mal and typical 3 c/s spike-and wave attacks, the attacks increased in duration from 2–3 to 25–110 seconds in a woman of 35 generalised symmetrical multiple spike and slow wave bursts increased from one every 5–10 minutes to one every 5–30 seconds; in a man of 61 bilaterally synchronous and symmetrical 2–3 c/s slow wave runs increased from one every 15–60 seconds to one every 5–10 seconds in a man of 68 with left-sided anterior temporal focal spikes the increase was from 1 spike every 5–10 seconds to one every 2–3 seconds

In each group of seven one patient was without anticonvulsants, and the other six were on their usual medication.

The effect of chlorpromazine becomes noticeable within about 15 minutes It appears to run roughly parallel with the oncoming drowsiness.

The findings suggest that chlorpromazine by the intravenous route can increase the abnormal epileptic' activity of the brain as seen in the E.E.G They suggest that caution may be advisable in treating epileptic patients with the drug

A detailed report of the investigations with special regard to the use of chlorpromazine as a stimulating agent in E.E.G work will be published elsewhere

Mapperley Hospital,
Nottingham WALTER FABISCH

HEROIN

SIR,—Your editorial statement after Mr Southwood's letter of June 11 suggests that unless the manufacture of heroin is prohibited in this country the success of efforts to deal with addiction elsewhere would be prejudiced Such a ban can help to control addiction only if heroin legitimately made in Britain is getting illicitly into the hands of addicts No evidence that this is happening has been nor is it likely to be, produced Surely the medical profession are justified in demanding such evidence before accepting the limitation of liberty involved by the ban especially since Dr Wand in your report of his defence of the Government's action admits that it may lead to an increase in suffering however slight that may be.

In the United Nations publication *Bulletin on Narcotics* and in other United Nations documents, evidence may be found which leads to the conclusion that legally manufactured heroin supplies a negligible amount of the world's illicit traffic and that British sources supply none whatever Some other relevant facts and conclusions from the same sources are these

(1) The clandestine manufacture of heroin from opium and crude morphine is child's play' and such manufacture is an important source of illicit heroin

(2) As long as opium and morphine are available illicitly it will be impossible to control heroin production and addiction

(3) The U.S.A has recently suffered a serious exacerbation of heroin addiction affecting even school-children despite a ban on heroin now of thirty years standing The suggestion that results will appear only when the heroin ban is universal cannot be maintained in the light of the known facts on the sources of illicit heroin

(4) That the only way to abolish heroin addiction is to remove weaknesses in the control systems of opium producing countries which are at the root of the trouble

The main events leading to the present action may be summarised as follows

In 1924 a committee of the House of Representatives of the U.S.A. met to consider the heroin problem which was very serious then and since It was concluded that the medical use of heroin was negligible compared with its evil effects, and the drug was banned Since then international organisations have repeatedly toyed with the idea of a universal ban

At the 1931 Conference for the Limitation of the Manufacture of Narcotic Drugs at Geneva proposals to ban heroin entirely and to ban its export from producing countries were made The British delegate opposed both measures.

In 1954 at the 243rd meeting of the Commission on Narcotic Drugs a vote was taken on a proposal that all countries should be recommended to ban heroin The British delegate abstained because he had received no specific instructions; he was confident however that the United Kingdom would give the resolution favourable consideration. This has now been done but still the medical profession has been given no evidence that the ban will help the international problem

It might be suggested that we should support the United Nations and set a good example in this respect but it surely cannot be argued that to impose a useless prohibition which infringes medical liberty and may cause suffering would favourably impress anybody

The second part of the Government ban that on export will be beneficial in lessening opportunity for theft in transit and since heroin can be made so easily legitimate consumers overseas will not be deprived

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[4] Tardieu G., Tardieu, C Le système nerveux végétatif Paris 1948.

[5] Decourt P Pr Méd 1954 62 511

[6] Vaughan G I Leiberman D M. Cook L C *Lancet* May 28 1955 p 1083

[7] Lomas, J Boardman R. H Markowe M *Ibid* June 4 1955 p 1144

I suggest, Sir, that we should not, in fact, "prejudice the success" of the international effort to prevent heroin addiction "if we dissociate ourselves from it," and that "a few sufferers should be allowed a little extra suffering" (as Dr Wand suggests) only when evidence is produced showing that their suffering will lead to a greater good Until then it is to be hoped that the medical profession will continue to oppose this administrative ban

Loss of heroin in this country will be loss to patients not loss to addicts

University College Hospital
Medical School,
London, W C 1

D R LAURENCE

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LUNG CANCER AND SMOKING

SIR,—Mr Gould's comments (June 4) upon a relatively unimportant statistical test of significance that we used in our paper of three years ago should not be allowed to obscure the accumulated evidence upon the association between smoking and lung cancer Since 1950 there have been published the results of thirteen other similar inquiries, carried out in six countries, all but one of them have revealed a substantial excess of smokers among the patients with lung cancer compared with the control group, and all of them have shown a large excess of heavier smokers amongst the lung-cancer patients The evidence from these numerous retrospective inquiries has been well supported by the preliminary results of two prospective inquiries In short, whether or not one interprets the weight of evidence as denoting causation, it is impossible, in our view, to suggest that the association is not firmly established

In fact, the statistical argument employed by Mr Gould is incorrect The figures, the significance of which he questions, are

	No of men with lung cancer	*No of men without lung cancer*
No of smokers	1350	1296
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He argues that if N is the number of men from whom the lung cancer patients are drawn, p_1 is the proportion who smoke, and p_2 is the proportion who have lung cancer, then the expected number of lung cancer patients who smoke will be Np_1p_2 and the range within which the observed number is likely to lie will be $Np_1p_2 \pm \sqrt{Np_1p_2}$ With the figures he assumes for N, p_1, and p_2 (90,467, 0 975 and 0 015 respectively), he deduces that the expected number of smokers with lung cancer would be $1323 \pm \sqrt{1323}$—i e, would lie between 1287 and 1359 The error lies in his choice of formula for the standard deviation of a proportion. The formula $\sqrt{Np_1p_2}$ is a valid approximation to the standard error of the number of lung cancer patients who smoke, in an *unrestricted* random sample of N males (the approximation being valid because p_1p_2 is small) But we are concerned with the number of smokers found in a sample of 1357 lung cancer patients, and this has a standard error of $\sqrt{1357p_1(1-p_1)}$ This would agree with the previous formula if p_1 were small, since $1357 = Np_2$, but in fact p_1 is estimated as 0 975 The appropriate estimate of the range is, therefore, $1323 \pm \sqrt{(1357)(0\ 975)(0\ 025)}$ The observed number should, then, lie between 1317 and 1329 (though we would prefer to take limits of twice the standard deviation on either side of the expected number, giving 1311 and 1335)

The error would have become clear if Mr Gould had applied his formula to estimate the expected limits for the number of *non smokers* which might be observed by chance among the lung cancer cases He would then have found that the small number of non smokers was statistically highly significant A formula which gives different results when applied in two different ways to the same set of figures might reasonably be considered a trifle unconvincing

London School of Hygiene
and Tropical Medicine W C 1

RICHARD DOLL
A BRADFORD HILL.

INVESTIGATION OF TONSILLECTOMY

SIR,—Your issue of June 4 (p 1184) referred to a proposed experiment approved by the South East Metropolitan Regional Hospital Board The same wording of this proposal has found its way into the local press "At Farnborough Hospital, Kent, and perhaps other hospitals in that area, 1000 children on the tonsils waiting list will be chosen for the trial 500 will have their tonsils removed and 500 will not The health of the two groups in the succeeding year will then be compared"

Farnborough Hospital is only one of several hospitals covered by the Bromley Group Hospital Management Committee, and the expression "in that area" leads both medical and lay public to assume that the consultant staff of these other hospitals may have agreed to such a plan, and, further, that this experiment would inevitably delay the admission of the 500 children in the control group, unless the waiting list were more than twelve months

The consultant staff of the Children's Hospital, Sydenham, would be glad if, through your columns, it could be made clear to practitioners in the area that no such inquiry is contemplated at this hospital, nor has the matter ever been referred to the medical staff committee, or to any individual member Since ethical considerations have been raised in the national press in connection with this proposed inquiry, it seems to us advisable to have the matter clarified in this way

Children's Hospital,
Sydenham, London, S E 26

D F ELLISON NASH
Senior Surgeon

*** Mr Ellison Nash's letter was shown to Dr Duncan Leys, whose name was quoted as being in charge of the investigation, and he replied

"Ethical considerations in this study differ in no way from those of other therapeutic trials If the value of the operation, which has a definite but undetermined morbidity, were unquestionable, there would be no need to undertake an investigation"—ED L

TUBERCULOSIS IN EIRE

SIR,—In your issue of June 11 (p 1221) you quote from an extremely interesting review of tuberculosis in Eire from 1949 to 1953 The figures show a very considerable increase in the number of patients treated, coupled with figures which show a very great fall in number of deaths

If the death-rate can be reduced to zero or nearly so, is it safe to say that tuberculosis has been eliminated from Eire? Surely with the figures being what they are in Eire, England, and Scotland, the measuring rod for tuberculosis should be amended so that the true criterion for tuberculosis is *not* the death-rate but the number of sick individuals

High Wycombe,
Bucks

L PITCHER

FOOD IN MENTAL HOSPITALS

SIR,—The mental hospitals have good reason to be grateful to the King Edward's Hospital Fund, and, as a member of a hospital management committee, I would like to congratulate the secretary of the Fund's hospital catering and diet committee on his article which you published last week

It is very true that large sums must be spent on equipment, and staff, before a civilised standard of catering can be reached in mental hospitals It is also true that an improvement well worth having can be made by spending even a few shillings per head more on food As little as 2*s* per head per week, spent on things that do not need cooking, such as milk, butter, cheese, fruit, salad, and marmalade, can make a very great difference

Even this modest sum involves an extra expenditure of £5200 a year on 1000 patients, and H M C members are timid about overspending

If the publicity you are giving to the disgracefully low standards that exist at the moment induces the [illegible] to feed the patients and damn the consequences I feel sure that the Treasury pig will be [illegible] to jump over the stile.

London, S.W.3 E. L. M. [illegible]

THE DIFFICULT APPENDIX

SIR,—I am grateful to Dr Horwitz (May 14) for drawing my attention to Dr Charles McBurney's original article[1] which has recently been made available to me through the courtesy of the librarian of the Royal Society of Medicine.

In 1940 Sir Hugh Devine[2] mentioned a position of the appendix in which it extends under the terminal part of the ileum and may give rise to "umbilical pain and other atypical symptoms." He went on: "anomalous forms of acute appendicitis, too, are most difficult to diagnose in their early stages and are the cause of many failures to make a prompt diagnosis." In abdominal diagnosis he reiterated the importance of a deep tender spot of visceral tenderness in localised inflammation, which is elicited by pressure of the finger point.

In 1937 Bowen[3] recommended palpating the iliac fossæ by trying to dip deep down on to the posterior abdominal wall with the fingers bent on the hand. He found that the local [illegible] pain usually at or about McBurney's point. "In rare cases local tenderness and resistance are entirely absent anteriorly in the lumbar region and on pelvic examination. In one case of which I have notes, the appendix was in a fossa behind the mesentery where it was securely hidden from prying hands."

In 1948 Sir Zachary Cope[4] warned against temporising and recommended always to make a very thorough attempt to elucidate the problem when the patient is seen for the first time. "It is only by thorough examination that one can propound a diagnosis, and if the early stages of the disease are to be recognised note must be taken of the earliest symptoms."

He recorded that if the appendix be situated behind the cæcum, or behind the end of the ileum and common mesentery, the inflammatory process will be somewhat masked by the gut lying in front. The place where deep tenderness can almost always be elicited is the spot just below the middle of a line joining the anterior superior iliac spine and the umbilicus. This roughly corresponds with the base of the appendix. Tenderness over McBurney's spot is not so constant. This tenderness appears to be localised actually in the appendix itself for the site of the pain varies somewhat according to the position of the appendix.

In 1889 Dr McBurney published 8 cases illustrating the new and successful treatment of early removal of the inflamed appendix. "All will acknowledge that every case of appendicitis may, so far as the cleverest observer can tell, have to pass many very dangerous obstacles before reaching the smooth water of a comfortable abscess. For my part, I would endeavour to ensure safety early before reaching the rapids rather than trust to finding my way blindfolded through a dangerous passage." His case 7 was tethered retro-mesenteric followed by temporary ileus.

He indicated the site of the greatest pain, determined by the pressure of one finger, as between 1½ in. and 2 in. from the anterior spinous process of the ilium towards the umbilicus. "No one will dispute that if we could so improve our methods of diagnosis that we could recognize within the first few hours the serious nature of many cases, we would operate in these cases at once, willingly preferring to incur the risks of an operation rather than face the certainty of death from septic peritonitis. How may we improve our methods of diagnosis? At present I see no clearer road than the exploratory incision permitting a direct inspection of the parts and a complete study of the disease."

No reference was made to the literature in my article of April 9 which recorded local experience of early acute appendicitis in its various forms and physiological manifestations, with appropriate deep tender spots. These are grouped in the form of a square each 1½ in. from Zachary Cope's spot which is just below the middle of a line joining the anterior superior iliac spine and the umbilicus. The lower right hand corner of the square [illegible] of appendix abscess but this is a complication [illegible] not included. The picture is completed by the outlying spots which are described.

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The seat of the greatest pain determined by the pressure of one finger must remain a cardinal point in diagnosis.

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Obituary

REGINALD LANGDON LANGDON-DOWN

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AMONG medical families and traditions the Langdon Downs of Normansfield hold an honoured place. For three generations they have been responsible for this home for mentally defective children, and as its medical superintendent for some forty years Reginald Langdon Down, the senior representative of the second generation, made a considerable contribution to the scientific understanding and humane treatment of mental defect.

His father, J. L. H. Langdon Down, F.R.C.P., came up from Devonshire to study medicine at the London Hospital, where he eventually joined the staff. In 1868, with the help of his wife, he founded Normansfield as a home where mental defectives would be treated as members of a family. He allocated each small group of patients to the care of a single nurse who slept in their room. This system was successfully continued at Normansfield until recently. From small beginnings the home grew till it was able to accommodate 200 patients, and with it grew its founder's reputation. He was the first to recognise and name mongolism, which is known in Russia as "Langdon Down's disease."

Reginald was born in 1866, and from Harrow he went to Trinity College, Cambridge, where he took a first class in the natural sciences tripos in 1888. He continued his medical studies at the London Hospital, qualifying in 1892. After serving as an assistant demonstrator of anatomy and a house-physician at the London he took the M.R.C.P. in 1894 and settled in private practice in Teddington. He was already drawn to the family specialty and two years later on the death of his father he and his brother Percival took over Normansfield. He continued the tradition of a family relationship with the patients in which the staff share. Later when Normansfield became a limited company he insisted on resigning his M.R.C.P., though to the regret of his colleagues. Today the home is part of the National Health Service

I suggest, Sir, that we should not, in fact, "prejudice the success" of the international effort to prevent heroin addiction "if we dissociate ourselves from it," and that "a few sufferers should be allowed a little extra suffering" (as Dr Wand suggests) only when evidence is produced showing that their suffering will lead to a greater good Until then it is to be hoped that the medical profession will continue to oppose this administrative ban

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AMONG medical families and traditions the Langdon-Downs of Normansfield hold an honoured place. For three generations they have been responsible for this home for mentally defective children, and as its medical superintendent for some forty years Reginald Langdon-Down, the senior representative of the second generation, made a considerable contribution to the scientific understanding and humane treatment of mental defect.

His father, J. L. H. Langdon Down, F.R.C.P., came up from Devonshire to study medicine at the London Hospital, where he eventually joined the staff. In 1868, with the help of his wife, he founded Normansfield as a home where mental defectives would be treated as members of a family. He allocated each small group of patients to the care of a single nurse, who slept in their room. This system was successfully continued at Normansfield until recently. From small beginnings the home grew till it was able to accommodate 200 patients, and with it grew its founder's reputation. He was the first to recognise and name mongolism, which is known in Russia as "Langdon Down's disease."

Reginald was born in 1866, and from Harrow he went to Trinity College, Cambridge, where he took a first class in the natural sciences tripos in 1888. He continued his medical studies at the London Hospital, qualifying in 1892. After serving as an assistant demonstrator of anatomy and a house-physician at the London he took the M.R.C.P. in 1894, and settled in private practice in Teddington. He was already drawn to the family specialty, and two years later on the death of his father he and his brother Percival took over Normansfield. He continued the tradition of a family relationship with the patients, in which the staff share. Later when Normansfield became a limited company he insisted on resigning his M.R.C.P., though to the regret of his colleagues. Today the home is part of the National Health Service.

but the family tradition continues and the superintendent is a nephew, Dr Norman Langdon-Down

Langdon-Down was a man of lucid and analytical mind with corresponding powers of expression He confined his considerable abilities within a limited field, and did all that he did well and graciously Many of his outside interests were closely linked with his specialty He was drawn into the inner counsels of the British Medical Association as an adviser on the evidence to be submitted to the Royal Commission on Lunacy Law and Mental Disorder, and he presided over a committee set up to study psycho-analysis, and served on the Central Ethical Committee His services were recognised by election as a vice-president of the association For many years he was physician to the National Association for the Welfare of the Feeble-minded, and by his work as chairman of the governors of Hampton Grammar School and as a governor of Epsom College he showed that he understood the needs of normal as well as defective children He was an acknowledged expert on Oriental porcelain, pottery, and furniture, and was himself a keen painter in water-colours

Dr Langdon-Down's first wife died in 1917 Five years later he married again, and his second wife died in 1942 He leaves two sons and two daughters He died on May 29 at the home which he shared with his daughter and son-in-law, Sir Russell Brain

JOHN EVERIDGE

O B E , F R C S

Mr John Everidge, consulting urological surgeon to King's College Hospital, died at his home in London on June 8

From King's College School he went to study medicine at King's College Hospital, qualifying in 1908 When he gained his F R C S in 1912, he was the youngest fellow He held resident appointments and the Sambrooke surgical registrarship at King's before he joined the R A M C in 1914 During the war he served with distinction as a surgical specialist, with the rank of major, and was mentioned in despatches and appointed O B E Soon after demobilisation, in 1919, he was appointed to the honorary staff of King's College Hospital as assistant urologist

On the retirement of Sir John Thomson-Walker in 1929, he was appointed senior urologist and gave up general surgery, which was at that time linked with the junior urological appointment, but he did not give up his interest in general surgery

He was consulting urologist to Queen Alexandra Hospital, Millbank, and he worked at many smaller hospitals, including the Sutton and Cheam Hospital and the Carshalton War Memorial Hospital He was one of the original consultants appointed to London County Council hospitals In the late war he was one of the senior staff at the Horton Emergency Hospital

Mr Everidge was long a prominent member of the urological section of the Royal Society of Medicine and he served as president during the early part of the late war He was a founder member of the British Association of Urological Surgeons, of which he later became hon treasurer, but his slight deafness made him refuse the presidency

J G Y-B writes "At King's Everidge's splendid teaching, imparted with wit without crudity, attracted large throngs to his clinics In surgery he was a pioneer in transurethral prostatic surgery as long ago as 1927, and played a part in the development of the modern resectoscope Always helpful to his juniors, it was a matter of pride to him that so many of his old house-surgeons held consultant posts His charm was outstanding and he was held in the highest esteem by his colleagues and friends, patients were devoted to him by virtue of his sympathy

"Outside his work he had many interests—lawn tennis in his early days, and in more recent years golf at Epsom and Deal, while many weekends were spent fishing with urologist friends He was a member of the Flyfishers' Club He always remained young, in surgery by keeping up to date with new procedures, and in private life by his enjoyment of all student activities, dances, and fast cars His after-dinner speeches were polished and entertaining He will be greatly missed as a surgeon and as a friend"

His wife was formerly Miss Kathleen Robertson, and he leaves a son and a daughter

ROBERT ARTHUR LYSTER

M D Birm , B Sc. Lond & Birm

During the first quarter of this century Robert Lyster's name was prominent among the planners of the personal health services, particularly the school medical service, and his colleagues, especially those of the older generation, will learn with regret of his death at the age of 82 at his home in Bournemouth

He began his studies at Mason College, Birmingham, taking the B SC Lond with double honours in 1893 He went on to study medicine at Queen's College and at Birmingham University, qualifying in 1900 He was early drawn to preventive medicine, and he held various lectureships in hygiene in Birmingham, including one at the Birmingham and Midland Institute Meanwhile he took the D P H in 1901, the B SC in public health of Birmingham University in 1905, and the M D in 1908 He had already entered the public-health service and he obtained varied experience while holding appointments with varied authorities, including those of the West Riding of Yorkshire, Sutton Coldfield, Warwickshire, and Handsworth

In 1908 he was appointed county M.O H for Hampshire, and during the next twenty-one years his work was centred on, but not confined to, Hampshire In his own area he set up sanatoria, an institution for mental defectives, and child-welfare centres, and over the years he also became a member of the medical board of the Lord Mayor Treloar's Hospital at Alton, of the faculty of medicine and board of studies in hygiene of the University of London, and of the Central Midwives' Board, a president of the Society of Medical Officers of Health, and editor of *Public Health* H C M W, who has helped us in these recollections, recalls that Lyster's dynamic personality and strong convictions often made him appear intolerant of other people's opinions, but adds that "many of his colleagues and assistants will look back with gratitude to the guidance and help that they received from him while he held office in the public health service"

In 1929 Dr Lyster retired, rather earlier than is usual, for he hoped to go into politics He stood as a Labour candidate in the parliamentary elections of 1929 and 1935, but he was unsuccessful. He had, however, been elected to the Bournemouth borough council and he later concentrated on local government, serving for many years as a valued and knowledgeable member of the council's health committee

EDWARD CECIL CLEMENTS

C B E , M.R C.S

Group-Captain Clements, formerly consultant in ophthalmology to the Royal Air Force, died on May 19 at the age of 81

He qualified from the Middlesex Hospital in 1901, and after a period of study under the elder Lang at Moorfields he went into private ophthalmic practice at Lincoln

As a Territorial officer he was called up as soon as war broke out in 1914, and it was during his service with the R A.M C that he observed that people in certain occupations, such as bank clerks and those using precision instruments, tended to lose their power to maintain binocular single vision and to become affected by eye-strain, which could not, as a rule, be compensated by correcting spectacles Appreciating that this was really an imbalance of binocular vision, or heterophoria, he instituted eye exercises and found that these improved or reduced the eye-strain After he was transferred to the Royal Flying Corps, and later to the Royal Air Force as an ophthalmologist, he noticed the same condition in pilots and realised its importance in judging distance when landing aircraft

He used the Maddox rod for diagnosis and Black's amblyoscope in treatment, and in 1918 he formed his school of heterophoria at the aviation candidates' medical board in London By this contribution to the growing study of orthoptics he undoubtedly reduced the wastage of pilots, both trained and undergoing training

In 1919 Clements was appointed to a permanent commission in the medical branch of the Royal Air Force as a squadron leader. A year later he was promoted to wing-commander and in 1928 to group captain. He continued to practise as an ophthalmic specialist throughout his service and he was appointed consultant in ophthalmology in 1931. A colleague who worked with Clements at Holly Hill, Hampstead, in the 20's recalls with awe his untidiness and with affection his kindness and generosity. He was created C.B.E. in 1934 and retired later in that year.

In recent years the approach to heterophoria has changed, but there can be no doubt as to the value of the work Clements did in the early days of aviation ophthalmology.

The photograph of Dr C. W. Buckley which we published last week was by Navana Vandyk, London.

Diary of the Week

JUNE 19 TO 25

Monday, 20th

POSTGRADUATE MEDICAL SCHOOL OF LONDON, Ducane Road, London, W.12
4 P.M. Dr Lewis Dexter (Boston): Cor Pulmonale.

Tuesday, 21st

ROYAL COLLEGE OF PHYSICIANS OF LONDON, Pall Mall East, S.W.1
5 P.M. Dr Kenneth Perry: Pulmonary Disease Associated with Metallic Oxide. (Ernestine Henry lecture.)
INSTITUTE OF DERMATOLOGY, St. John's Hospital, Lisle Street, W.C.2
5.30 P.M. Dr O. L. S. Scott: Hypostatic Ulcers.

Wednesday, 22nd

INSTITUTE OF DERMATOLOGY
5.30 P.M. Dr R. W. Riddell: Subcutaneous Mycotic Infections.

Thursday, 23rd

POSTGRADUATE MEDICAL SCHOOL OF LONDON
4 P.M. Dr J. C. Gilson: Rheumatism and Lung Disease.
INSTITUTE OF DERMATOLOGY
4.30 P.M. Dr Henry Haber: *Reticuloses.*

Friday, 24th

POSTGRADUATE MEDICAL SCHOOL OF LONDON
2 P.M. Mr John Bruce: Regional Enteritis.
4 P.M. Mr I. McG. Moffatt: Use of the Ophthalmoscope in Medicine. (Second of two lectures.)
ROYAL SOCIETY OF MEDICINE, 1, Wimpole Street, W.1
8.15 P.M. *Obstetrics and Gynæcology.* Mr A. L. T. Easton, Dr Peter Andrews, Mr Stanley Way, Mr Anthony Charles: Carcinoma of the Vulva.

Saturday, 25th

RADCLIFFE INFIRMARY, Oxford
11.15 A.M. Dr Neville Oswald: Chronic Bronchitis.

Appointments

[illegible], H. C., M.R.C.S., D.P.M.: deputy medical superintendent, Rampton Hospital, Retford, Notts.

[illegible], R. S., M.B. Glasg., D.P.M.: whole-time asst. psychiatrist (S.H.M.O.), St. Nicholas Hospital, Gosforth, Newcastle upon Tyne.

[illegible], J. J., M.D. Camb., M.R.C.P., D.P.M.: asst. physician, department of psychological medicine, Guy's Hospital, London.

[illegible], L. L. W., M.B. Edin., F.R.C.S.E.: surgeon, Leith Hospital, Edinburgh.

[illegible], JOYCE C., M.B. Lond.: asst. geriatrician (S.H.M.O.), Northampton and Kettering H.M.C.s

[illegible], JACK, M.B. Glasg., D.O.M.S.: whole-time ophthalmologist, Royal Infirmary, Edinburgh.

[illegible], W. F. K., M.B. Belf., D.A.: part-time anæsthetist (S.H.M.O.), Banbridge and Dromore and South Down H.M.C.s

[illegible], CONSTANTIN, M.B. Lwow, D.A.: consultant anæsthetist, South Shields H.M.C.

[illegible], K. W., M.R.C.S., D.A.: asst. anæsthetist (S.H.M.O.), High Wycombe and district H.M.C.

[illegible], R. D., M.R.C.S., D.P.H.: deputy M.O.H., deputy principal school M.O., and deputy port M.O., Ipswich.

[illegible], P. M., M.B. Edin., F.R.C.S.E.: consultant surgeon, North West H.M.C., Northern Ireland Hospitals Authority.

[illegible], L. B., M.B. Lond., F.R.C.S.E.: whole-time asst. consultant plastic surgeon, Whiston Hospital, Alder Hey Children's Hospital, and the Royal Southern Hospital.

[illegible], FRANCIS, M.B. Lpool: asst. M.O. and deputy M.O., borough of Buckingham, Bletchley, Linslade and Newport Pagnell urban districts, and Buckingham, Newport Pagnell and Wing rural districts.

[illegible], A., M.B. Sheff., D.A.: whole-time anæsthetist, Moorgate General Hospital, Rotherham, Yorks.

[illegible], L. A., M.D. Aberd., M.R.C.P.: consultant physician (pediatrics) based on Glenburn Wing, Woodend Hospital, Aberdeen.

Amended notice.

Notes and News

MENTAL NURSING FILMED AGAIN

THOSE who saw *The Troubled Mind*[1] need not fear that *Light through the Clouds*—a film about nursing at The Retreat, York—will take them over the same ground; for though the two films have the same main theme (that of a young girl entering mental nursing) and both are skilfully photographed and well scripted, they are complementary rather than overlapping. In the first, emphasis is often on patients and their symptoms; in the second it is on methods of treatment. Neither perhaps gives a complete picture of mental nursing (if such a thing is possible) but together they come very close to doing it.

The Retreat is an exceptional hospital with one of the longest traditions in this country of humane care of the mentally ill; and *Light through the Clouds* conveys well the atmosphere of friendship and coöperation in which the work there is done. The rate of staffing is high—100 nurses to 270 patients—which may account for the unusually peaceful tempo at which things seemed to move. The early sequences show well that the nurse in a mental hospital learns all the techniques of sick nursing which would come her way in a general hospital—a fact not always appreciated by general nurses. Then follow examples of forms of treatment used specifically on mental patients—insulin coma, electroconvulsion therapy, and psychotherapy. The work of the physiotherapy and X-ray departments is also lightly sketched. Members of the nursing staff take the parts of patients, and certainly give no cause for alarm to young prospective nurses who may see the film. Some of the recreations of the nurses are shown, and the beauty of the setting of The Retreat, as well as the fine old house from which it has grown, are given their proper value. The commentary ends with a direct appeal to the young girls who might be interested—"the Janets and the Kathleens"—to consider mental nursing as a career.

The production and photography are by Mr C. Harold Wood, and the film has been made under the direction of Mr P. Thomas Oliver and Mr of Alan H. Pickard who also wrote the commentary.

A DOCTOR AND THE RAIL STRIKE

A DOCTOR in Birmingham has declined to see one of his patients, the wife of a railway striker, until the strike is over.[2] The patient had an appointment to see him privately, but after the strike began the doctor wrote to her husband:

> "I am afraid my principles prevent me from seeing patients who are on strike except in cases of emergency. . . . If you will 'phone for an appointment when the strike is over I will try to fix a convenient date."

The doctor is reported to have said that nothing in his refusal was detrimental to the patient. She was not ill now and the appointment was for a routine examination.

University of Oxford

Surgeon Rear Admiral James Hamilton has been appointed director of postgraduate medical studies for five years from Oct. 1.

On June 4 the degree of D.M. was conferred in absence on R. W. Gilliatt.

University of Cambridge

On May 28 the following degrees were conferred:

M.B.—William Atherton, A. E. L. le Thierry,* J. F. Walker.
* By proxy.

University of Durham

Dr Donald Court, reader in child health, has been appointed to the chair of child health in the Newcastle division of the university in succession to the late Sir James Spence.

Dr Court graduated in medicine at the University of Birmingham in 1930 and later became house-physician at Great Ormond Street Hospital and pædiatric registrar at Westminster Hospital. In 1935 he took the M.R.C.P. and the D.C.H. Before taking up his present appointment at Newcastle he held a Nuffield fellowship in child health. In 1947 he proceeded to his M.D. degree. He contributed the chapter on tuberculosis in *Garrod, Batten and Thursfield's Diseases of Children* and he has also published papers on the health of nurses. He is a joint author of recent publications on infantile mortality in Newcastle.

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1. *Lancet*, 1954, ii, 1291.
2. *Times*, June 11, 1955.

Royal College of Physicians of London

On Tuesday, July 12, at 5 P M, at the college, Pall Mall East, S W 1, Lord Amulree will give the F E Williams lecture, on Modern Hospital Treatment and the Pensioner

Royal College of Surgeons of England

At a meeting of the council held on June 9, with Sir Harry Platt, the president, in the chair, Mrs Mitchiner presented two badges of office for the vice presidents, given in memory of her husband, Philip H Mitchiner The medical directors-general of the Army and the Royal Air Force presented the Mitchiner medal to Colonel W R M Drew, late R.A M C, for his contributions to medicine in the Army, with special relation to the teaching of tropical medicine, and the Lady Cade medal to Squadron Leader P Howard for his experimental work in the development of partial pressure suits and pressure breathing equipment

The following were coöpted to the council for the year 1955-56, representing various branches of practice

Dr O C Carter, general practice Mr A B Nutt, ophthalmology Dr E Rohan Williams, radiology Mr Myles L Formby, oto laryngology Dr Frankis T Evans, anæsthetics Prof F C Wilkinson was invited to act as the representative of dental surgery

The following examiners were appointed for the coming year

Fellowship —Ophthalmology E A Blake Pritchard Anatomy Mary F Lucas Keene, Lambert C Rogers R. J Last Sir Cecil Wakeley Applied Physiology and Pathology Geoffrey Hadfield, Albert Hemingway J L D'Silva H A. Magnus

Diploma of M R C.S, L R C.P —Elementary Biology Alan Fish G F H Foxon Anatomy F W T Morris A J Heriot W J Hamilton Physiology Esther M Killick B D Wyke Midwifery R G Maliphant, W R Winterton, H H Fouracre Barns Ian Donald Pathology Joseph Bamforth, A C Cunliffe, Sir Cecil Wakeley, E G Tuckwell

Diplomas of fellowship were granted to the following

A B McGrigor I L Gregory * Peggy K Orton, Cecilie Greig, D A Watson, R W Bottoms Gordon Hadfield, G S Plaut P K Pybus John Humphreys Alexander Gol, A E Richardson K R I de Belder, J E H Pendower, G H Jantet Leon Friedmann R. H Baird † J C B Serjeant, N E Brand E V Peipman W A Baker Mihir Kumar Guha Thakurta, F J Hedden F W Parry Madan Mohan Chawla T J Thwaite A H Toyne, Betsy Brown, G P Debenham Hyman Gaylis, N A A Myers, Sheroo Darabsha Broacha H H Chesterfield-Evans, † C I Phillips, Bhabani Bhattacharyya, B L Cornish Kevin Cronin, Jackie Jacob, M L H Lee, H G Lowe G D H Shawe Leslie Simon N V Addison T J Claffey * C N d'E Eastes Frank Ellis W F Gordon, Benjamin Ho W M Keynes J P Maddern P F Mountford J K Oyston Harry Piggott, D R. Richard T M Robinson W G Taylor, G D Tracy H T G Williams G S M Botha * D J Brain J A C Brown Ranes Chandra Chakravorty D A Cooper J B Doss Mohamed Saad El Din Ed Dars W B Fleming, P A Freeman S B Joshi R H Kernutt I A Loeb, I L McVey, Satyendra Nath Basu Roy, C G Tulloh R. G Williams K P Abel, Syed Mohamed Alwi Alhady J G Corson D O Cropley J A Myburgh Nergish Rustomji Patel, G J Schnitzler S R. Shar W W Slack V H Smith A. B Vivian, A F Wallace D W Warren D G Falles J F H Graff Alan Jessup, Cyril Shaldon D D Arnold, Jyotishchandra Narendrarai Joshipura

* In otolaryngology † In ophthalmology

Diplomas of membership were granted to the following

B M G Clarke A Gibbons Janet Goodall

The following postgraduate diplomas were granted jointly with the Royal College of Physicians

D M R D —N H Aldridge L J du Preez David Edwards Shirley F Entrican W C Heron Kazi Shamsul Huque Catherine V Krafft Omar Bin Din, W M O Purcell Arun Rattarangsi, M J Ryan, M M Schechter Jogendra Prasad Sinha G C Stavrakis

D M.R T —H D Batt P E Bodkin, T B Brewin J C Courtney Hazel E Davidson Hung Chiu Ho Youssef Nasrallah I M Shulman A J Ward

D Path —Leonard Bernstock, D A L Bowen Moses Levene Leslie Michaels N E Rankin P D Roberts, T P Telfer T A White

Royal College of Physicians of Ireland

At a meeting of the college held on June 3, with Dr Edward Freeman, the president in the chair, the following were admitted to the fellowship

P B B Gatenby S D McGrath M A Majekodunmi M. G Nelson H O Flanagan P P O'Malley

The following were admitted to the membership

F A Farrelly E W Knox J Lowry, D H Merrin, Eleanor T Rolston

Royal Australasian College of Physicians

On May 11 the following were admitted to the honorary fellowship of the college Sir William Slim the governor general of Australia the Rt Hon Robert Menzies, the prime minister and Sir Russell Brain, F R C P

Royal Society of Medicine

At the 150th anniversary dinner of the society on June 7 the Duke of Edinburgh was made an honorary fellow an received a copy of the commemorative history of the societ written for the occasion by Dr Maurice Davidson, wh presented the volume The President, Sir William Gilliatt told the Duke that one of the privileges he would now enjo would be to borrow eight volumes at any one time from th R S.M library, which, Sir William said, might fairly be calle the National Medical Library of the Commonwealth, for, the society's 10,000 fellows, nearly 2000 lived oversea Like many similar institutions the R S M was much troubl by the rising cost of books, bindings, and paper, but the were good hopes, the President went on, that the generos of friends and the loyalty of fellows would enable them place their finances in an impregnable position Propos The Society, the Duke recalled the time when, in its earlier days, Robert Liston's 30 second leg amputation was as much the talk of the day as the 4 minute mile was now, Turning to the modern scene, he said he was sure that the whole essence of medicine lay in the personal relationship between doctor and patient, and that was why he was particularly glad to be present at an occasion where Sir William presided—though, he hastened to add, he had never actually been a patient of his In his response, Sir Francis Walshe, immediate past president of the society, spoke of the immense pride and pleasure of all the fellows in having the Duke with them, "in a double sense one of our number" The Guests, cordially proposed by Sir Arthur Porritt, drew sparkling replies from Lord Salisbury and Lord Adrian

Medical Association for the Prevention of War

Prof L S Penrose, F R S, will open a discussion on his book *The Objective Study of Crowd Behaviour* at 8 P M on Wednesday, June 22, at 45, Russell Square, London, W C 1 Dr Norman Glaister will be in the chair

Oxford Graduates' Medical Club

The summer dinner of this club will be held in Oriel College, Oxford, on Friday, July 1, at 7 P M, with Dr F G Hobson in the chair Members may bring medical men or women as guests Tickets (35*s*) may be had from Mr Ronald Macbeth, F R C S, department of otolaryngology, Radcliffe Infirmary, Oxford.

Hospitals' Symphony Orchestra

This orchestra is to give a concert at B.M.A House, Tavistock Square, London, W C 1 on Saturday, June 25, at 7 30 P M The programme will include Haydn's Trumpet Concerto, Brahms's Fourth Symphony, and works by Dvořák Sibelius and Berlioz Tickets (10*s*, 7*s* 6*d*, 5*s*, and 3*s* 6*d*) can be had from Mr Mitchell, the concert manager, St Thomas's House, S E 1

United States Supreme Court

On June 6 the court found that Dr John Peters, senior professor of medicine at Yale University, had been wrongfully dismissed as a "security risk" from his post as a government consultant in 1953 The court's majority opinion ordered the Civil Service Commission to strike from its records a finding by the old loyalty review board that there was a reasonable doubt as to Dr Peters's loyalty

Canadian Nuffield Fellows

Nuffield travelling fellowships in medicine have been awarded this year to the following Canadian doctors Dr H R Brodie, Dr W R N Lindsay, Dr D G Marshall, and Dr J A Palmer A travel grant has been awarded to Prof R L de C H Saunders, head of the department of anatomy, Dalhousie University, to study micro radiographic equipment in England

CORRIGENDA *A Ruler for Use in Electro encephalography and Electrocardiography* —In this article (June 4, p 1158) the third sentence in the third paragraph should read "Should lines other than those immediately adjacent to the vertical be used, the figures representing C P S and seconds are divided by 2 and 3 and multiplied by 2 and 3 respectively"

Pembury Hospital, Kent —In recording (June 4, p 1184) the dedication of a memorial window at this hospital, we gave the name of Mr J F Carter Braine incorrectly

THE INCIDENCE OF LEUKÆMIA IN ANKYLOSING SPONDYLITIS TREATED WITH X RAYS

A PRELIMINARY REPORT

W. M. COURT BROWN
M.B., B.Sc. St. And., D.M.R., F.F.R.

JOHN D. ABBATT
M.B. Edin., D.M.R.

MEMBERS OF THE EXTERNAL SCIENTIFIC STAFF, MEDICAL RESEARCH COUNCIL, DEPARTMENT OF MEDICINE, POSTGRADUATE MEDICAL SCHOOL OF LONDON

IN a discussion of a paper on the long-term evaluation of the treatment of ankylosing spondylitis with X rays (Robinson and Lampe 1948), Graham stated that 2 of his patients so treated had died of leukæmia. Since 1949 van Swaay (1954) has collected data on 7 people who had died from leukæmia and who also had X-ray treatment for ankylosing spondylitis.

In recent months an investigation has begun into the death-rate from leukæmia among people suffering from ankylosing spondylitis and treated with X rays. This investigation is being continued under the auspices of the Medical Research Council's working party on leukæmia research, and, while its final conclusions will not be reached for some considerable time, the findings to date are felt to be sufficiently important to warrant a preliminary report.

Provisional Findings

An attempt has been made to obtain information regarding the treatment of ankylosing spondylitis from all the radiotherapy centres of both England and Wales and of Scotland. The following information has been sought from each of fifty-eight different centres:

(1) The total number of patients treated with X rays for ankylosing spondylitis from 1940 to 1954 inclusively.
(2) The number of patients treated for the first time in each year of this fifteen-year period.
(3) The age and sex distribution.
(4) The number of patients given more than one course of X-ray treatment.
(5) The number of patients reporting back at intervals for medical examination.
(6) Records of any patient who had developed leukæmia, aplastic anæmia, or myelofibrosis.

Preliminary data have been collected on 9364 patients treated in thirty-seven Radiotherapy Centres, these including all except *four* of the *major centres*. The criterion for the inclusion of a patient in this series has been a diagnosis of ankylosing spondylitis at the time of his or her first X-ray treatment, even though subsequent to this the diagnosis may have been found to be in error.

It will be seen in the subsequent analyses of age and sex distribution, &c., that in each instance the number of patients analysed is *smaller than the total number* concerning which information has been obtained. The cause of this discrepancy is that many of the centres have not made a return of all the information that was requested. For this reason it has been found necessary in order to estimate the number of cases of leukæmia that might be expected to occur to make a number of assumptions in regard to the whole population based on analyses carried out on parts of the population. To avoid any tendency to underestimate the expected number of cases of leukæmia as these assumptions have had to be made, a number of safeguards have been adopted as will subsequently become clear.

Age-distribution

The age-distribution is known for 2697 patients of both sexes and is given in table I. The ages referred to are those of the patients when they were seen in a radiotherapy centre for the first time.

Sex-distribution

The sex distribution is known in 4297 patients of whom 3679 are males and 618 are females. The ratio of males to females is 5·95 : 1.

Patients kept under Observation

From the information supplied by seventeen radiotherapy centres concerning 3085 patients, an estimate has been made of the proportion of patients who are kept under observation after the conclusion of their X-ray treatment. Of the total of 3085 patients 1731 (56%) are periodically reporting back to the various centres for examination or are known to have died whilst the remaining 1354 patients (44%) have been lost sight of, either as a result of failure of the patients to report back to these centres or because periodical medical examinations have been dispensed with on account of the continuing good health of the patients.

TABLE I—AGE DISTRIBUTION OF 2697 PATIENTS

—	0–14	15–24	25–34	35–44	45–54	55–64	65–74	75–
Absolute numbers	4	415	1000	733	363	160	25	1
% of total	0·15	15·39	37·08	27·16	13·46	5·93	0·92	0·04

More than One Course of X-ray Treatment

In a proportion of patients it is found necessary to give more than one course of X-ray treatment to keep the disease under control. In a series of 2361 patients 797 (33·8%) were given more than one treatment course.

Patients who got Leukæmia

Records have been obtained of 25 patients who have developed leukæmia (table II) and this total of cases is likely to be incomplete as many of the 9364 patients—perhaps as many as 44%—have not been kept under observation. But it does not necessarily follow that the number of deaths is as incomplete as was the follow-up of the patients, because the fact of death may have been more readily reported back to the radiotherapy centre concerned. On the other hand it must be borne in mind that a number of patients are likely to fail to report back to the centres because they have died, but the centres themselves, unaware of the cause for non-attendance, may record them as being "lost sight of."

4 patients are included in whom leukæmia and ankylosing spondylitis were considered to be co-existent when the patients were given X-ray treatment for the first time.

TABLE II—RECORDED CASES OF LEUKÆMIA

Total	Age-distribution (years)		No. with apparent co-existence of leukæmia and spondylitis	No. having one treatment course only	No. having more than one treatment course	Latent period† (months)	
	Range	Mean				Range	Mean
25 (21)	17–65	36	4 (4)	6 (5)	15 (12)	[illegible]–161	74

Types of leukæmia

Clinical		Cytological			
Acute	Chronic	Lymphatic	Myeloid	Monocytic	Unspecified
19	6	2	11	8	4

Figures in parentheses refer to numbers of patients notified to the Registrar-General as dying from leukæmia.

† Time interval between start of first course of treatment and the clinical recognition of leukæmia, in those patients who did not apparently have co-existent leukæmia at the time of first treatment of their ankylosing spondylitis.

Expected and Observed Deaths from Leukæmia

The death-rates from leukæmia in England and Wales have increased steadily since 1940 (table III) There has been a similar but less consistent upward trend in the Scottish death rates

In this preliminary report an approximate estimate of the number of deaths from leukæmia which might have been expected to occur among all the 9364 patients has been made in the following way

TABLE III—DEATH RATES FROM LEUKÆMIA FOR ENGLAND AND WALES AND FOR SCOTLAND, 1940–1953 (REGISTRAR GENERAL)

Year	Deaths per million living persons			
	England and Wales			Scotland
	Male	Female	Both sexes	Both sexes
1940	30	23	26	38
1941	29	22	25	28
1942	34	24	28	27
1943	38	25	30	32
1944	38	26	31	32
1945	40	29	34	32
1946	41	30	35	34
1947	38	32	35	32
1948	40	31	35	30
1949	44	35	40	39
1950	47	37	42	39
1951	47	41	44	43
1952	52	41	46	41
1953	53	44	48	38

The numbers of patients known to have been aged 0–14, 15–24 25–34, &c , shown in table I have been multiplied by the age specific death-rates for men in England and Wales in 1953 The rates for men have been used because the greater proportion of the treated patients whose sex was known were men (86%) and because the death-rate from leukæmia was, in general, slightly higher in men than in women The rates for 1953 were used because the death-rate from leukæmia has been rising throughout the period studied (table III), and by using the latest (and highest) rates available the expected number of deaths will be overestimated rather than underestimated

If it is assumed that the age-distribution of the whole 9364 patients is the same as that of the 2697 patients analysed in table I, then the total number of deaths, expected to have occurred in one year can be obtained by multiplying the sum of the expected numbers for each group by the factor 3 472 (9364/2697)

At this point a further consideration must be taken into account The patients were treated up to fifteen years ago and, therefore, have been exposed to the risk of dying for a number of years During these years the patients have also aged and, depending upon their age-groups, have been exposed to a greater or lesser risk of dying as they aged In a series of 6187 patients from twenty-six radiotherapy centres, only 12% of the patients entered the series during the first quinquennium and as many as 49 3% entered it during the last quinquennium If it is assumed that all the patients in the series have, on the average, been observed for ten years, the expected number of leukæmia deaths for the whole period will not be underestimated and will be obtained by multiplying by a further factor of ten Also, on the average, all the patients will have aged five years during their period of observation, so that instead of multiplying the numbers of patients in the age-groups 0–14, 15–24, 25–34, &c., by the mortality-rates for these groups themselves they must be multiplied by the mortality-rates for the age-groups five years in advance, i e , 5–19, 20–29, 30–39, &c

The total number of leukæmia deaths expected for the whole period is, therefore, the sum of the expected numbers in the individual age-groups (0 1125) multiplied by 3 472 × 10—that is, 3 9

Only those deaths observed in the series and certified as being due to leukæmia can be compared with the estimate of the expected number of deaths since the estimate of the expected number of deaths is based on the causes of death certified to the Registrar General 21 of the observed cases of leukæmia were certified as dying from leukæmia If it is assumed that no other cases of leukæmia have occurred in the untraced sections of this population then the ratio of observed deaths to expected deaths is 21 3 9 or 5 4 1 If, however, it is assumed that the same proportion of leukæmia deaths has occurred in the untraced section of the irradiated population as in the traced section, then the ratio of observed to expected deaths may well be as high as 37 3 9 or 9 5 1

12 of the patients certified as dying from leukæmia were given more than one course of X ray treatment From the information provided by thirteen centres about 2361 patients, 33 8% were found to have had more than one treatment course If it is assumed that this proportion is the same in the whole population of 9364 patients, the ratio of observed deaths to expected deaths is 12 1 32 or 9 1 1 It is not possible to make an estimate of the proportion of those patients given more than one treatment course who are untraced, and consequently an estimate cannot be made of the total number of cases of leukæmia that may have occurred in that group *

Discussion

The object of this preliminary report is to call attention to the high number of deaths from leukæmia amongst a series of *patients suffering from ankylosing spondylitis* and treated with X rays Other causes of death, such as aplastic anæmia, will be dealt with in a later communication

In this report a number of assumptions have been made, especially in regard to the age distribution Thus, it is possible that the age distribution of ankylosing spondylitis differs in the two sexes and it is likely that the mean age of these patients will have increased somewhat in the latter part of the fifteen year period when fewer patients were being referred for treatment from the Armed Services It is, however, probable that any tendency that these assumptions may have had to underestimate the expected number of deaths is more than offset by the use of the highest recorded death-rate from leukæmia in this calculation, by the absence of any correction for sex-distribution, and by the assumption of a mean period of observation of ten years

4 patients have died in whom leukæmia and ankylosing spondylitis were considered to be co existent before the institution of X ray treatment Also 1 patient died of leukæmia two months after the start of X ray treatment, and his leukæmic state may have been present when treatment was begun, though unrecognised Bearing in mind that the estimated number of leukæmia deaths—i e , 3 9—is likely to be artificially high through the adoption of a number of safeguards, and that it also relates to a ten-year period of observation, it is not possible to exclude some association between the two diseases No attempt has been made to review the diagnoses in any of those cases in which both leukæmia and ankylosing spondylitis were said to be co existent If both diagnoses are correct in each of the 4 cases, there is a possibility that persons suffering from ankylosing spondylitis are more liable to develop leukæmia than the general population of England and Wales of the same age distribution and sex distribution On the other hand, it is possible that in some cases errors in diagnosis have been made, and that the pain and disability suffered by the patients were solely due to the leukæmic processes If this were so the argument in favour of an association between the two diseases would be less strong Bearing

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* If it is assumed that the same proportion of the patients receiving more than one course of X ray treatment is untraced as is the case for the whole population, then the ratio of observed to expected cases of leukæmia would be as high as 21 1 32 or 15 9 1 It is, however, probable that patients receiving multiple courses of treatment are more likely to be kept under observation than those given only a single course of treatment

in mind these possibilities it is now pertinent to examine the evidence suggesting that X irradiation may have been a major cause of the unexpectedly high numbers of patients found to have leukæmia.

15 patients who had more than one course of X-ray treatment developed leukæmia, while 6 patients had leukæmia after only one course of treatment. It has already been shown that 33·8% of a series of 2381 patients had more than one treatment course. Assuming that the same proportion of the total population of 9364 patients had more than one course, then 1 patient in every 211 patients treated in this way developed leukæmia in contrast to 1 patient in every 1033 patients who had only one course of treatment. If these groups of patients are comparable with regard to sex, age, and duration of observation, the difference between them in the incidence of leukæmia is appreciable (χ^2 = [illegible], n = 1, P < 0·001). This finding that the incidence is higher among those treated more than once is only to be expected if X irradiation is an important factor in determining the occurrence of leukæmia, for it is reasonable to suppose that the greater the number of treatment courses the greater the risk of leukæmia.

Before the X-ray treatment can be finally accepted as a major cause two further considerations must be examined. In the first place it is not possible to be certain that some of the patients who developed leukæmia after a second course of treatment were not in fact given this second course on account of pain and disability caused by the leukæmic process, this not being recognised at the time. If this were the case then the significance of the difference between the two groups would be diminished and might even disappear. While in the cases that have been reported there is no evidence that this has occurred, it is a theoretical possibility that must be considered. In the second place it is fair to assume that those patients requiring more than one treatment course were suffering from a more severe form of ankylosing spondylitis than those requiring only one course of treatment. There is no evidence, either clinical or statistical, to refute an argument that the severer form of the disease is not itself associated with a greater predisposition towards the development of leukæmia than the less severe form.

It is clear that on the evidence presented so far no final conclusions can be reached on the part played by X-ray therapy in the production of the increased numbers of cases of leukæmia in this series of cases of ankylosing spondylitis. It is, therefore, relevant at this point to discuss the reported examples of the development of leukæmia following the exposure of persons to ionising radiations, apart from the purpose of treating malignant disease.

It is now recognised that an increase has occurred in the death-rates from leukæmia in both Nagasaki and Hiroshima, attributable to the atomic explosions occurring over those cities in 1945 (Folley et al. 1952, Lange et al. 1954, Moloney and Kastenbaum 1955). Merklen et al. (1925) reported the development of chronic myeloid leukæmia in a woman seven years after X-ray treatment for uterine fibromata, and Gerbis (1943) and Lynch (1951) reported acute myeloid leukæmia following the use of X rays in the treatment of non-malignant skin lesions. More recently Simpson et al. (1955) have claimed a statistically significant increase in the incidence of leukæmia and of carcinoma of the thyroid in a series of children given X-ray treatment in infancy because of suspected enlargement of the thymus gland. There is evidence also that occupational exposure to ionising radiations may be associated with an abnormally high death-rate from leukæmia. In particular, a number of reports establish a good case for such an increased death-rate amongst physicians practising radiology (Ulrich 1946, March 1950, Peller and Pick 1952).

The evidence from the literature suggests that exposure to ionising radiations can be leukæmogenic in man. Leukæmia has occurred in association with an acute whole-body exposure following the explosion of a nuclear device, with various forms of radiotherapy, and with chronic occupational exposure. On this basis and in spite of the difficulties in the interpretation of the present findings it is perfectly reasonable to conclude that some, perhaps the great majority, of the cases of leukæmia found in this series have occurred as a result of X-ray treatment. The fact that sufferers from ankylosing spondylitis may be unusually susceptible to the development of leukæmia has also been stressed, but only further research can evaluate the relative parts played by the possible susceptibility of these patients to leukæmia and the X-ray treatment.

In spite of these findings it would be wrong to withhold X-ray treatment from those suffering from ankylosing spondylitis. It is common knowledge that the life-expectancy of many of these patients is reduced by their disability, and most authorities agree that radiotherapy has in many instances a beneficial effect. What is certain, however, is that no one should be treated with X rays unless the diagnosis is clearly established, and that a second course of X-ray treatment should not be given unless absolutely necessary.

Summary

(1) An inquiry is being made into the death-rate from leukæmia amongst patients suffering from ankylosing spondylitis and treated with X rays.

(2) A series of 9364 patients treated from 1940 to 1954 inclusively has been analysed and the expected number of deaths from leukæmia in this series has been calculated on the basis of the male age-specific death-rates from leukæmia in England and Wales for 1953.

(3) The observed deaths from leukæmia have been found to be at least five times, and possibly as many as ten times, the expected number of such deaths, and amongst those patients given more than one course of X-ray treatment the observed deaths are probably at least nine times those expected to occur.

(4) Evidence has been put forward which suggests that patients with ankylosing spondylitis may be unusually susceptible to the development of leukæmia. But also it is likely that the incidence of leukæmia is appreciably raised amongst those patients given more than one course of X-ray treatment.

(5) Reviewing the above findings in the light of a number of reports in the medical literature it is concluded that some, if not the majority, of the observed cases of leukæmia may be attributable to X irradiation.

(6) Further investigation is necessary to confirm these findings.

We are grateful to all those radiotherapists and other colleagues who have kindly supplied us with data. A more detailed acknowledgment will be made in a later communication.

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REFERENCES

Folley, J. H., Borges, W., Yamawaki, T. (1952) *Amer. J. Med.* 13, 311.
Gerbis, H. (1943) *Dtsch. med. Wschr.* 69, 510.
Lange, R. D., Moloney, W. C., Yamawaki, T. (1954) *Blood*, 9, 574.
Lynch, F. W. (1951) *Arch. Derm. Syph. (Chicago)* 63, 603.
March, H. (1950) *Amer. J. med. Sci.* 220, 282.
Merklen, L., Wolf, Neel (1925) *Bull. Acad. Méd. Paris*, 93, 361.
Moloney, W. C., Kastenbaum, M. A. (1955) *Science*, 121, 308.
Peller, S., Pick, P. (1952) *Amer. J. med. Sci.* 224, 154.
Robinson, W. D., Lampe, I. (1948) *Ann. rheum. Dis.* 7, 245.
Simpson, C. L., Hempelmann, L. H., Fuller, L. M. (1955) *Radiology* (in the press).
Ulrich, H. (1946) *New Engl. J. Med.* 234, 45.
van Swaay, H. (1954) Personal communication.

THE NATURAL HISTORY OF PERIPHERAL TUBERCULOUS LYMPHADENITIS ASSOCIATED WITH A VISIBLE PRIMARY FOCUS

F J W Miller
M D Durh , M R C P , D C H
LECTURER IN PÆDIATRICS

Joan M Cashman *
M B Durh , D C H
RESEARCH ASSISTANT

DEPARTMENT OF CHILD HEALTH, ROYAL VICTORIA INFIRMARY, NEWCASTLE UPON TYNE

KNOWLEDGE of the relation of the time and site of the primary tuberculous infection to its manifestation and observation of the ultimate result are particularly important in the study of peripheral tuberculous lymphadenitis, which is still often said to be "most often a *manifestation of generalised tuberculous infection*" (American Trudeau Society 1954)

Since 1947 we have been studying primary tuberculosis of skin and mucosa Primary infection on these sites has proved to be much more common than at first seemed possible, and 28 cases have been described (Miller 1953) Since then further cases have been seen and, if we include those with visible primary lesions of tonsils and mouth, we have 40 children with visible primary tuberculosis who have been under observation for a minimum of two years In this group the site, and, within narrow limits, the time of primary infection are known, and we have observed the behaviour of the regional glands in neck, groins, and axillæ Though the cases were first seen in differing stages of evolution, we think they form the basis of a study of the natural history of peripheral tuberculous lymphadenitis

Therefore we report here the changes in the glands in these 40 children , but before doing so we must explain our diagnosis of primary tuberculosis and distinguish between clinical and experimental work—i e , between probability and proof In clinical work we do not impose our own conditions on the material studied and we deal with reasonable probabilities Thus if we are to prove that any manifestation of tuberculosis is part of a primary complex—i e , primary focus and regional glands—we should observe the tuberculin conversion of the patient as well as demonstrate a primary tuberculous focus and its associated regional glands This proof is usually absent apart from occasional, almost accidental, observations But if we can show by a combination of clinical, histological, and bacteriological techniques that a tuberculous focus exists, and that the regional glands are the site of caseous change, we can use the pathological studies of Ghon and Terplan to support the probability that we are witnessing a primary infection in the person concerned (Terplan 1940)

It is strange that there is no agreement on the pathogenesis of tuberculous lymphadenitis, and that we cannot find an accurate account of the natural history of this condition The main reason seems to be that no worker has described a series of cases in which the time of the primary infection, whether recent or remote, was known accurately, and most accounts do not discuss the presence or absence of manifestations of tuberculosis elsewhere in the body

The best published report that we have found is that of Thompson (1940), also working on Tyneside, who reviewed 324 cases of tuberculosis of peripheral lymph-nodes His purpose was more to describe the pathogenesis than the natural history, but he did conclude

> "That whatever method [of treatment] was employed the disease usually followed a prolonged and relapsing course, tending ultimately to local healing with a greater or lesser degree of scar formation accompanied by contraction with fibrosis or calcification of the affected lymph glands "

He said also

> " There is some doubt whether gross tuberculosis occurs in lymph nodes infected other than during the primary phase, " and " it follows that the group of lymph nodes initially involved should indicate the portal of entry of the infection "

We feel that by observing a group with a known pathogenesis and time of infection we have the opportunity to make an accurate record of the natural history in a small well defined group of cases

Clinical Cases

The distribution of the primary foci and the regional glands is shown in figs 1 and 2 All the children were tuberculin-positive, the tuberculous nature of the process was proved, and all the children were observed for at least two years after infection

Tuberculous lymphadenitis is still common in the North east of England, and 224 cases (2%) were seen in 11,400 admissions to the children's department of the Royal Victoria Infirmary in the seven years 1947–53

Descriptions of representative lesions in skin and mucosæ have already been given In table I nos 1–23 and 25–28 refer to the same cases the original case 24 has been excluded because he was an adult, and another has been substituted (Miller 1953)

The behaviour of the glands can perhaps best be described by answering five questions How do they present ? How many soften to form abscesses, and how long do they take to do so ? How many calcify and in how long ? What are the complications of the visible primary complex ? How long do the glands take to heal after spontaneous rupture has occurred, and what is the period of morbidity ?

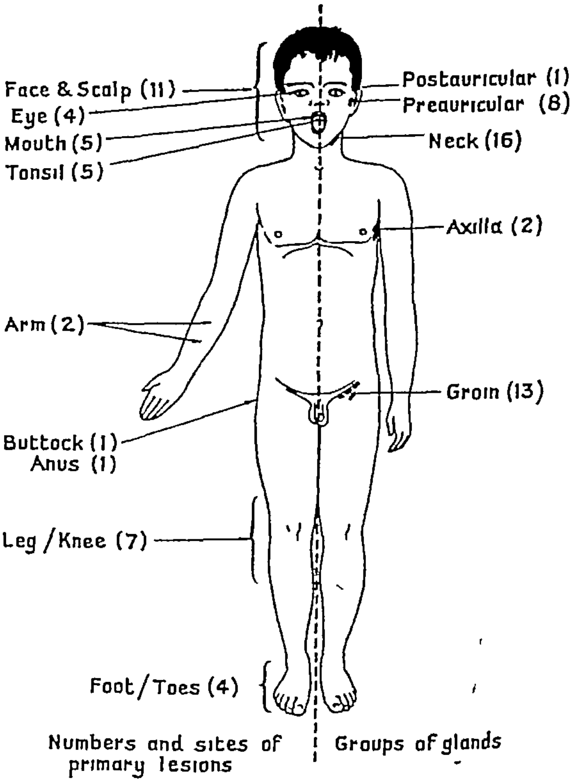

Fig 1—Distribution of sites of primary infection and groups of glands affected

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* Working with a grant from King's College Rag Appeal Fund

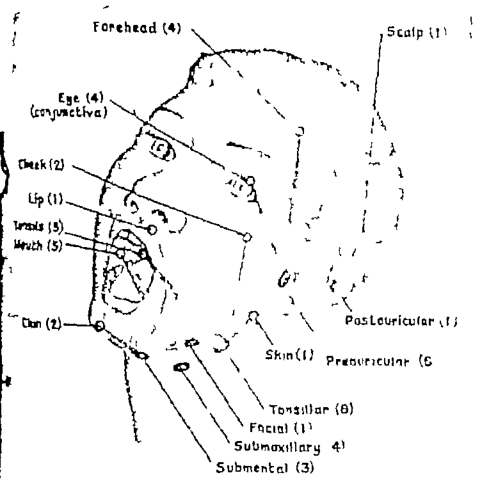

Fig. 1—Relationship between site of primary infection and regional glands first infected in head and neck.
○ = site of primary infection; **O** = first regional gland

How do the glands present?

Table I shows that 23 cases came to hospital after the accidental discovery by the mother or the child of a painless gland swelling; in another 4 the onset was much more acute with rapid swelling, pyrexia and some pain simulating an acute pyococcal adenitis; of these in case 20 the onset followed a cut by a piece of broken glass and was so rapid with such acute swelling that a double infection was almost certain.

In 7 cases a painless primary lesion was the first complaint, whereas in another 5 the primary lesion and the glands were noted simultaneously; the remaining child was admitted to hospital with miliary tuberculosis and the primary focus then discovered.

The absence of pain often seemed to delay consultation with the doctor; no less than 23 of the glands were already soft when first seen, and in 10 of these the abscesses had already ruptured. In the remaining 17 cases the glands were still firm.

In 8 of the 12 cases where the primary lesion alone or simultaneously with the gland had been the first complaint, an abscess had already formed when the child was first seen in hospital.

Less than half the children (15) had any systemic illness at the time of the appearance of the glands; pyrexia varied from a slightly raised temperature lasting a few days to a definite illness—the "fever of onset"—lasting three weeks (Wallgren 1948).

TABLE I—SYNOPSIS OF DATA OF 40 CASES OF PERIPHERAL TUBERCULOUS LYMPHADENITIS

Case no.	Site of primary lesion	Primary gland group	State of gland when first seen	Time from infection to softening	Course and surgical management	Pyrexia at onset	First symptom
1	Skin	Femoral	Firm	4 weeks	Aspirated	–	Swelling in groin
2	Cheek	Preauricular	Firm	5 mos.	Ruptured	–	Spot on face and swelling in front of ear
3	Knee	Inguinal	Soft	Not known	Ruptured	+	Acute inguinal adenitis
4	Heel	Inguinal	Ruptured	8 weeks	Incised	–	Inguinal adenitis and lack of healing
5	Knee	Inguinal	Ruptured	Not recorded	Incised	–	Inguinal swelling
6	Foot	Inguinal	Soft	4 mos	Incised	+ (Injury)	Lack of healing after accident
7	Arm	Axillary	Soft	2 yr	Excised	–	Axillary adenitis
8	Toe	Inguinal	Ruptured	3 mos	Incised		Swelling in groin
9	Knee	Inguinal	Ruptured	8 mos	Excised	–	Red area on knee
10	Calf	Inguinal	Ruptured	3 mo	Excised	+	Acute inguinal adenitis
11	Knee	Inguinal	Soft	4–5 mos	Excised	–	Scab did not heal
12	Chin	Submental	Soft	3 mos	Aspirated	–	Swelling under chin
13	Anus	Upper inguinal (bilateral)	Ruptured	2 weeks	Aspirated	+	Swelling in groin
14	Chin	Submental	Ruptured	3 mos	Ruptured	–	Lesion on chin, submental abscess
15	Cheek	Tonsillar	Firm	11 weeks	Aspirated ruptured	–	Spot on face, tonsillar gland swelling
16	Forehead	Preauricular	Ruptured	1 month	Incised	Erythema nodosum	Wound did not heal
17	Forehead	Preauricular	Ruptured	3 weeks	Incised	–	Scab on forehead and abscess in front of ear
18	Scalp	Postauricular	Soft	5 mos	Ruptured	+ (Injury)	Postauricular abscess
19	Calf	Inguinal	Soft	Not known	Incised	Erythema nodosum	Ill on admission after measles
20	Foot	Inguinal	Firm	6 weeks	Excised	+	Septic foot and acute adenitis
21	Eye	Preauricular	Soft	8 weeks	Ruptured	–	Sore eye
22	Eye	Tonsillar	Firm	3 mos	Incised	Erythema nodosum	Swelling of tonsillar gland
23	Eye	Preauricular	Soft	8 mos	Ruptured	–	Chronic conjunctivitis
24	Buttock	Lower inguinal (bilateral)	Ruptured	4 weeks	Incised	–	Abscess in groin
25	Eye	Preauricular	Firm	6 weeks	Incised	–	Small swelling in front of ear
26	Mouth	Facial (supramandibular)	Firm	1[illegible] mos	Incised	–	Ulcer in mouth
27	Mouth	Submaxillary	Firm	6 weeks	Aspirated	+	Submaxillary swelling
28	Mouth	Submaxillary	Soft	10 weeks	Aspirated incised	–	Submaxillary swelling
29	Skin above lip	Submental	Firm	[illegible] mos	Ruptured	+	Swelling in neck
30	Skin below ear	Tonsillar	Soft	4 weeks	Incised	–	Swelling in neck
31	Forehead	Preauricular	Soft	32 mos.	Aspirated incised	+	Swelling of cut, swelling in front of ear
32	Forearm	Axillary	Soft	3 mos	Aspirated incised	–	Swelling in axilla
33	Forehead	Preauricular	Firm	11 weeks	Incised	–	Lump under jaw
34	Mouth	Submaxillary	Firm		Excised	–	Lump under jaw
35	Mouth	Submaxillary	Firm		Excised	–	Swollen jaw
36	Tonsil	Tonsillar	Firm		Excised	+	Lump in neck, pyrexia
37	Tonsil	Tonsillar	Firm	1 month	Incised	Erythema nodosum	Lump in neck
38	Tonsil	Tonsillar	Firm		Excised		Swollen gland
39	Tonsil	Tonsillar	Firm		Excised		Swollen glands
40	Tonsil	Tonsillar	Firm		Excised	–	Swollen gland

TABLE II—TIME FROM INFECTION TO ABSCESS FORMATION

Time (mos)	< 3	3–6	9	12	24	32	Unknown
No of cases	14	11	3	1	1	1	3

4 of these had erythema nodosum, and 4 others the acute reaction and severe lymphadenitis with pain simulating pyococcal infection (Miller 1952) In 23 there was either no alteration of health or it was so slight as to escape notice In 2 cases the tuberculosis was a complication of severe trauma received in a road accident The source of infection and the relationship to trauma have already been considered (Miller 1953)

29 of the children had radiographs taken of the chest and 11 had radiographs of the abdomen when they were first seen Calcification was not visible in any In case 14 a second active primary complex was seen in the lung, and case 19 had miliary tuberculosis These were the only cases with clinical evidence of tuberculosis other than the primary complex

How many glands soften and how long do they take to do so?

We have already stated that 23 of the glands had softened to form abscesses when they were first seen and the remaining 17 were firm 6 of the firm glands were removed by local dissection before an abscess formed In the remaining 11 abscesses formed, making a total of 34 abscesses in the 40 cases No less than 25 had softened within six months and 29 within a year (table II)

Of the 12 glands which were firm when first seen and went on to soften 3 were treated with streptomycin while still firm They diminished in size as the periadenitis resolved, but all ultimately softened—i e , all the glands not removed when firm eventually formed abscesses

In how many cases and after how long did radiographic calcification take place?

We were concerned to discover how many of our cases developed calcium in the glands, and when it appeared If all or most of these proved cases did so, the presence of calcium can be used in other series to support a diagnosis of tuberculosis and to estimate how long the infection has been present

In 28 of the 40 children visible calcium developed at the site of the regional lymphatic glands Of the 12 others 4 had the glands excised (3 before and 1 after softening had taken place), 1 died, and 2 have been infected just over two years Possibly we may yet detect calcium in these 2 and in some of those whose glands were excised (3 of the patients in whom the presenting glands were firm when excised have developed calcium in neighbouring glands), but we do not know why the remaining 5 do not show calcification—possibly all the caseous material was discharged

We were not able to radiograph each child annually, and we cannot set out a complete table of the time of the appearance of calcium from infection, but of 15 cases examined a year after infection only 4 had visible calcium, whereas 18 other cases appeared by the end of the third year, making a total of 22 from 35 examined, In 24 of the 28 cases calcium was present within five years of infection (table III)

Calcification is therefore to be expected in the regional glands of a primary lesion on skin or mucosa, and in our series was seen within our period of observation in 28 from 39 possible cases

36 of the children had radiographs of the chest and abdomen two or more years after infection Case 14 proved to have calcified hilar glands (this was the child who was known to have an active primary lesion in the chest at the same time as the primary lesion on the skin), the remaining chest films were clear Calcification was shown in three abdominal films Two of these were calcification in the deep iliac glands of 2 patients who had primary lesions on the leg and calcified inguinal glands The third was an unexpected finding in 1 of the children with a primary tonsillar infection and calcified cervical glands Of the remaining 4 children 1 died, and 3, though seen for two or more years after infection, did not attend for subsequent radiography

TABLE III—RELATIONSHIP OF CALCIFICATION TO TIME OF INFECTION

Radiographic examination of regional glands	Calcification	Years after infection								Total
		0	1	2	3	4	5	6	7	
First	Present		4	1	6	1	0	1	1	14
	Absent	14	5	4	1	0	1	0	1	
Subsequent	Present for first time		0	7	4	1	2			14
	Still absent		6	7	6	2	2	1	2	
	Total calcified		4	12	22	24	26	27	28	28

What are the complications?

1 child developed miliary tuberculosis and fatal tuberculous meningitis 3 of the 40 children had erythema nodosum, 3 others phlyctenular conjunctivitis, and 1 both No case of bone or joint tuberculosis has yet occurred in these 40 children

The commonest complication of the primary complex was abscess formation in the group of glands draining from the primary gland Secondary abscesses did not occur in the 6 children whose primary glands were removed by dissection before softening, but in the 33 others (excluding the death) there were 17 who had subsequent abscesses in glands further down the lymphatic chain These usually appeared within a year of the first abscess, but 1 appeared as long as seven years afterwards In 1 child, whose glands had not broken

TABLE IV—TIMES BETWEEN SOFTENING OF SUBSEQUENT ABSCESSES

Case no	First abscess	Interval	Second abscess	Interval	Third abscess	Interval	Fourth abscess	Interval	Fifth abscess
2	Preauricular	5 mos	Tonsillar						
5	Inguinal	6 mos	Deep iliac						
8	Inguinal	3 mos	Inguinal	30 mos	Deep iliac				
14	Submental	3 mos	Upper deep cervical						
16	Preauricular	2 mos	Tonsillar	6 mos	Post-sternomastoid				
17	Preauricular	11 mos	Tonsillar	1 month	Post-sternomastoid	17 mos	Upper deep cervical	3 mos	Preauricular
18	Postauricular	Local recurrence at intervals of 4 mos			10 mos, and 7 mos				
21	Preauricular	4 mos	Tonsillar						
22	Tonsillar	15 mos	Submaxillary						
25	Preauricular	5 mos	Tonsillar	6 mos	Post-sternomastoid				
26	Facial	6 mos	Submaxillary						
27	Submaxillary	13 mos	Submaxillary						
28	Submaxillary	3 mos	Submaxillary	3 yr	Tonsillar				
29	Submental	6 yr	Submaxillary						
31*	Preauricular		Tonsillar		Upper deep cervical				
33	Preauricular	3 mos	Tonsillar	15 mos	Post-sternomastoid				
37	Tonsillar	4 mos	Upper deep cervical						

* All softened simultaneously after measles 3 years after primary infection

TABLE V—TIME OF HEALING OF ABSCESSES

Abscesses	No of cases	Healed by first intention	Months from first operation (or rupture if no operation)				
			< 3	3–6	12	>12	Not recorded
Ruptured spontaneously							
Excised	2	1		1			
Incised or aspirated	8	1	4	[illegible]	1		
No operation	7		1	1		3	2
Softened but did not rupture							
Excised	5	4			1		
Incised or aspirated	12	1	5	3	1		2
Excised while firm	6	6					
Total	40	13	10	[illegible]	3	3	4

down for three years after primary infection on the forehead, the preauricular tonsillar and post sternomastoid glands all softened simultaneously after measles. of these 17 children had not only a second abscess but also a third further down the path of lymphatic drainage thus in case 33 the preauricular gland was first involved the tonsillar second and the posterior sternomastoid third. Case 17 had 5 abscesses (table IV)

How long does healing take after spontaneous rupture or operation, and what is the total period of morbidity?

All the cases eventually healed, but Thompson's opinion, quoted above of the natural course of tuberculous lymphadenitis with abscess formation seems to be valid still for the patients we see in hospital The glands which underwent spontaneous rupture, or were incised, were often slow to heal or broke down after initial healing So far as it affected the natural history, the management is described here

Of the 17 glands firm when seen 6 were excised and healed by first intention Of the 34 which softened 17 ruptured spontaneously (3 of which were firm when first seen and 4 soft), 2 were excised 8 incised or aspirated, and 7 allowed to heal without intervention The times taken for healing are shown in table V

TABLE VI—MORBIDITY

Duration (from infection) of inpatient and outpatient attendance at hospital

	Months				Years					
Time	0–6	6–12	12–18	18–24	2–3	3–4	4–5	5–6	6–7	7–8
Numbers	1	12	6	4	8	3	4		1	1

Of the remainder of the soft glands (8 firm and 9 soft when first seen) 5 were excised and 12 aspirated or incised. The duration of the sinus is shown in table V

Table V refers to the time taken for the first gland abscess to heal, but many children had more than one abscess, or their general condition made a long period of hospital care or outpatient supervision necessary The total duration of this morbidity is shown in table VI The time has been taken from infection to discharge from hospital, sanatorium or outpatient supervision and does not include visits made at our request 2 children are still attending—four years and two years after infection In some cases there was a gap of a year or two between hospital attendances. Moreover it is always possible that further complications may arise

Discussion

We have shown that the regional glands in 40 cases of primary tuberculosis with visible primary foci showed a striking tendency to soften Indeed all did so except those removed by dissection while firm In a few cases softening did not take place until more than a year after infection and after calcium had appeared The objection might be raised that because 23 of the glands had softened when first seen, the series was highly selected but there were 11 firm when first seen which were not excised and all these softened also

All the children except 3 came from "artisan or labouring" families. We do not know whether tuberculous adenitis in children of other social groups has the same tendency to soften but we do know that our experience in these 40 cases is in accord with the natural history of cases of tuberculous adenitis seen in our department, whether or not associated with a visible primary focus But the question always remains how often and in what circumstances does primary tuberculous peripheral lymphadenitis occur without softening but with the deposition of calcium? We have not yet a precise answer but we think it must be uncommon, probably occurring mainly in the upper social groups. Another piece of indirect evidence is the extreme rarity with which we find calcium in the neck in routine radiography without an overlying scar or sign of abscess We therefore feel that primary tuberculous peripheral lymphadenitis, as seen in the north east of England, is likely to proceed in most cases to abscess formation

If an abscess does form in the primary gland the possibility of an abscess in the next group of glands is high—17 in 33 (half our children) This prolongs the period of morbidity and makes a good cosmetic result more difficult to obtain

We have shown that calcification is visible in most of our cases and commonly appears in the second and third years after infection but possibly later Its appearance indicates the cause of a lymphadenitis of doubtful origin and allows an estimate of the time of infection where this is unknown Furthermore the presence of calcium can be used as a method of investigating the natural history of tuberculous lymphadenitis and we hope to continue this study by a review of some 350 cases seen in our department in seven years

Summary

We have studied the behaviour of the regional glands in 40 cases of primary tuberculosis of the skin and mucosa

In all the cases other than those 6 in which firm glands were removed by dissection the glands softened and abscesses formed In most cases this took place within six months of infection.

In 28 of 39 cases calcium was seen in the glands—none in the first year but in more than half the cases in two or three years In England the presence of calcium can therefore be used as diagnostic evidence and to estimate the time since primary infection

We wish to thank our colleagues in the department of child health and other departments of the hospital who referred cases of visible primary tuberculosis, and the members of the departments of bacteriology pathology, and radiology for their help

REFERENCES

American Trudeau Society (1951) *Amer Rev Tuberc* 70 910
Miller F J W (1952) *Brit med J* ii 1015
— (1953) *Lancet* i 5
Terplan, K (1940) *Amer Rev Tuberc* 40 suppl. 1
Thompson B C (1940) *Tubercle* 21 217
Wallgren A (1948) *Ibid* 29, 245

That was the trouble with courage perhaps: too many men had it The men in brown and the men in green the men in the Marauders and the men in the Junkers the men fighting each other with stones and clubs and axes and spears and swords and catapults and bowie knives and flint locks and Gatling guns and Bren guns and detonation bombs and fragmentation bombs and delayed fuse bombs and butterfly bombs and V 1 and V 2 and V 1000 They all had courage—did have it—would have it It was a terrible thing to admit perhaps but after enough years of killing and not being killed you got a little tired of courage There was so damned much courage in the world and so damned little wisdom '—J R ULLMAN *The White Tower* London 1954; p 375

USE OF ISOTOPE-LABELLED RED CELLS TO DEMONSTRATE INCOMPATIBILITY IN VIVO

P L MOLLISON
M D Camb , M R C P

MARIE CUTBUSH
B Sc Melb

From the Medical Research Council's Blood Transfusion Research Unit, Postgraduate Medical School of London

In selecting blood for transfusion it may be difficult to decide whether a reaction occurring in vitro implies that red cells will be destroyed in vivo For example, cross matching may reveal the presence of a specific antibody strongly active at low temperatures but doubtfully active at 37°C , in other cases all blood samples may react weakly with the patient's serum at 37°C, suggesting the presence of a non specific antibody In such cases there is a real need for a biological test to supplement tests in vitro

The earliest biological test introduced into transfusion work consisted simply in injecting a small volume of the donor's blood and looking for a clinical reaction A later refinement consisted in injecting the donor's blood in amounts of about 50 ml and looking for increases in bilirubin or for the presence of free hæmoglobin in the recipient's plasma (Wiener et al 1942) However, this test is not very sensitive (see Mollison 1951) Compatibility can be reliably assessed only by measurement of the survival of the injected cells

Until recently the survival of transfused cells could be measured only by differential agglutination This method is practicable only when donor and recipient belong to different ABO or MN groups and when an injection of at least 50 ml of the donor's blood can be made However, by labelling red cells with radioactive isotopes it is possible to measure the survival of very small volumes of cells In investigations reported here approximately 1 ml of red cells were labelled either with the isotope ^{51}Cr or with ^{32}P In addition to determining whether the red cells of prospective donors are compatible, this method provides a very useful means of discovering more about the action of blood-group antibodies in vivo

Methods

Labelling of Red Cells

About 1 ml quantities of red cells were labelled either with ^{32}P or with ^{51}Cr The ^{32}P method was essentially that described by Reeve and Veall (1949) as modified by Chaplin (1954) The ^{51}Cr method was that described by Mollison and Veall (1955) using ^{51}Cr with a specific activity of 5–10 mC per mg , the amount of Cr per millilitre of red cells was 2–10 µg

When two samples of cells, one labelled with ^{51}Cr and the other with ^{32}P, were to be injected, either the suspensions were made up to 25 ml separately or, more commonly, one sample of cells was added to the other and made up to a total volume of 25 ml with sterile ice cold saline solution The cells were kept cold until the time of injection, and then 20 ml of the suspension was injected from a calibrated syringe

Expression of Results

In all the cases reported below (except cases 1 and 4) the red-cell volume was determined by injecting the subject's own red cells or other compatible red cells labelled with either ^{32}P or ^{51}Cr From this determination the expected number of incompatible cells was calculated In the figures reproduced below the numbers of surviving cells are expressed as percentages of the expected figure

In cases 1 and 4, in which no compatible cells were injected, the red cell volume was deduced from the number of incompatible cells at zero time, determined by extrapolating the slope of elimination to the time axis

In calculating the survival of cells labelled with ^{32}P it was assumed that 1% of ^{32}P left the cells in each ten-minute period after the injection (Reeve and Veall 1949) , survival was measured by this method only for periods not exceeding one hour

In calculating the survival of cells labelled with ^{51}Cr no correction for loss of chromium was made during the first hour after injection, because it is known that the loss in so short a period is too small to be measurable When the survival of ^{51}Cr labelled cells was followed for periods exceeding one hour after injection, corrections for chromium elution were made from data published by Mollison and Veall (1955)—i e , it was assumed that about 6% of Cr was lost during the first 24 hours after injection, and that thereafter Cr eluted from the red cells with a half-period of about 55 days

Serological Tests

Unless otherwise specified, the antibody titres reported below refer to the results of indirect anti globulin (Coombs) tests Halving dilutions of the recipient's serum, taken immediately before the injection, were incubated with a sample of the cells used for injection In cases 2–5 sensitisation took place only in the presence of complement , therefore fresh " neutral " serum was added to each tube of the titration After incubation with the patient's serum the cells were tested with a range of dilutions of anti globulin serum The anti globulin serum used was one which had previously been shown to contain anti beta globulin as well as anti gamma globulin (see Crawford et al 1955)

Enzyme-treated cells were used for detecting Lewis antibodies (cases 2–4) and to demonstrate the characteristics of a serum containing anti P (case 5) The enzyme ficin was used, and the tests were made according to directions supplied by Dr. R E Rosenfield

One drop of a 1% ficin solution (in Hendry's buffer of pH 7 4) was added to nine drops of a 2% suspension of red cells , after 15 minutes' incubation at 37°C the red cells were washed once in saline solution and resuspended to a 2% concentration in fresh saline solution Two drops of the red cell suspension were mixed with two drops of the patient's serum , the mixture was examined for hæmolysis after one hour at 37°C

In each case the patient's serum was also tested for its ability to agglutinate cells suspended in saline solution at room-temperature and at 37°C In some cases, after the cells had settled in the tube, 20% albumin was substituted for the supernatant serum saline mixture and half an hour later the deposit was examined microscopically for agglutinates (Dodge 1952)

Results

Great variations in the rate of destruction of red cells were observed when incompatible cells were injected, the destruction tended to follow certain definite patterns

Elimination of Most of the Injected Cells within Ten Minutes

This pattern was observed after injecting Fy(a+) cells into case 1, whose serum contained anti Fy^a, and was also observed after injecting Le(a+) cells into case 2, whose serum contained anti Le^a

Case 1 —A man, aged 48, suffering from hæmophilia, had been transfused many times, and his serum contained the blood group antibodies anti-Fy^a and anti Rh During a period when he was in relatively good health and at work he was given small amounts of incompatible cells so that their survival could be studied Fy(a+) Rh negative cells from the same donor were injected on two occasions, being labelled with ^{51}Cr on the first occasion and with ^{32}P on the second As shown in fig 1, essentially the same pattern of elimination was observed on both occasions—i e , after a lag of two or three minutes the cells rapidly left the circulation , in the following five minutes 50% were removed, and after 20 minutes only 10% were left The remainder were more slowly eliminated

The two injections of Fy(a+) cells were given at an interval of two weeks , there appeared to be no immune response to

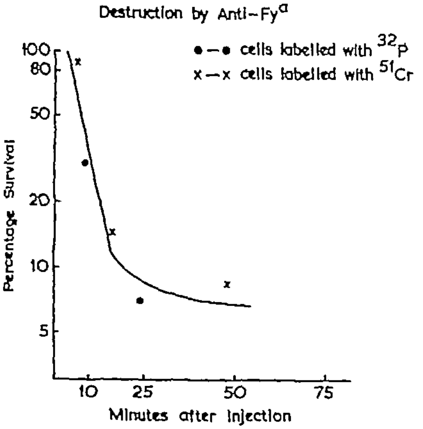

Fig. 1—Survival of Fy(a+) cells in case 1. The cells labelled with ^{32}P were injected two weeks after the cells labelled with ^{51}Cr; the same donor was used. The titre of anti-Fy^a was 1/8 on both occasions. The percentage survival is plotted on a logarithmic scale in this figure and in figs. 2-5 and 7.

the first injection, the titre of anti-Fy^a remaining at 1/8 throughout the period of the observations.

Case 2.—A man, aged 72, with subacute leukæmia received between May and July, 1954, blood from ten donors without reaction. In November, 1954, he was transfused with blood from two more donors (donors 11 and 12, see below). Four or five minutes after transfusion began he developed pain in the back, but this disappeared when the rate of the transfusion was slowed, and it did not reappear when the transfusion was speeded up. He was transfused with blood from four more donors (13, 14, 15, 16) during November without reaction, but on Dec. 1, after the transfusion of a further 250 ml. of blood (donor 17), he developed backache again, and the transfusion was discontinued. Shortly afterwards the patient passed urine containing hæmoglobin. Next day his serum was found to contain methæmalbumin, and his urine to contain methæmoglobin. During the next ten days he was transfused with five bottles of blood without incident.

On Dec. 16, 1 ml. of the fresh cells of donor 17, labelled with ^{51}Cr, was injected. The first sample, taken eight minutes after injection, contained only 20% of the expected count of cells. Further tests now showed that the patient's serum contained anti-Le^a and that donor 17 was Le(a+), as were donors 11 and 14.

A further test injection of Le(a+) cells (donor H. L.) was given when the anti-Le^a titre was 1/16: it was found that elimination was almost complete in ten minutes. When the numbers of surviving cells were plotted on a semi-logarithmic scale against time, it was observed that the points between about three and ten minutes fitted a straight line. This line, when extrapolated to 100% survival, crossed the time axis at about two and a half minutes, suggesting a short lag phase after injection (see fig. 2).

Le(a− b−) cells were relatively slowly eliminated—i.e., there was no significant change in their number during the few hours following injection. The survival of these cells was followed for two months, and it was found that their rate of elimination was only slightly greater than in normal recipients. It was presumed that the patient had a mild hæmolytic process, probably related to his leukæmia.

The patient's serum only weakly agglutinated Le(a+) cells. The antibody could be readily detected by the indirect antiglobulin test if the test was made in the presence of complement. The reactions were stronger when the patient's serum was incubated with cells at 37°C than when sensitisation was carried out at room temperature. After being heated to 56°C for twenty minutes the patient's serum no longer sensitised Le(a+) cells; its sensitising power was restored by the addition of fresh normal serum (lacking Le^a substance).

The antiglobulin reaction in this case (and in cases 3-5) did not depend on anti-gamma-globulin but on anti-beta-globulin in the rabbit serum. For example, the reaction was not inhibited by the addition of gamma-globulin but was inhibited by the addition of serum from a patient with agammaglobulinæmia (Crawford et al. 1955).

After treatment with ficin, Le(a+) cells were lysed by the patient's serum. Great variation was found among the reactions of Le(a+) cells from different donors; the cells could be classed as having 'strong' or 'weak' Lewis antigens, judged by their susceptibility to lysis and by their degree of sensitisation to an antiglobulin serum after exposure to the patient's serum. In comparative tests the cells of donor H. L. gave very weak reactions; nevertheless, as fig. 2 shows, they were very rapidly eliminated in this patient.

Rapid Elimination of a Proportion of the Injected Cells within Ten Minutes; Much Slower Elimination of the Remainder

This pattern was observed after injecting Le(a+) cells into cases 3 and 4, whose serum contained anti-Le^a. It was also observed after injecting P-positive cells into a patient with anti-P (case 5); in this case the elimination of the P-positive cells could not be prevented by warming the cells to 37°C before injection.

Case 3.—A woman, aged 19, had had severe hæmorrhage requiring transfusion at the time of parturition. She had never previously been transfused and had never been pregnant before. Her present infant (at the age of two weeks) was Le(a−) and had no Le^a substance in its saliva. The patient received blood (about 2500 ml.) from five donors and was noticed to be jaundiced next day. However, the possibility that the jaundice was related to the administration of blood was not seriously considered until ten days later. It was then found that the patient's serum contained anti-Le^a (titre 1/8) and that one of the five donors was Le(a+).

This patient's serum had the same general characteristics as the serum of case 2 but reacted less strongly in vitro with Le(a+) cells than did the serum of case 2. Similarly, when test injections of Le(a+) cells (donor H. L.) were given they were less rapidly eliminated (see fig. 2). During the ten minutes after the injection two-thirds of the cells were removed from the circulation; however, 20% of the cells were still present after 25 minutes, and no further decrease took place in the following 50 minutes. The cells had been labelled with ^{32}P, and their subsequent survival could not be estimated accurately; however, from the amount of ^{32}P present at 24 hours it was estimated that at least 10% of the cells were still present.

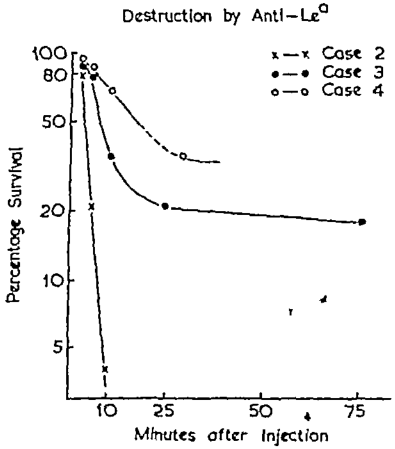

Fig. 2—Survival of Le(a+) cells from donor H. L. in cases 2-4. In case 4 the slope of elimination has been represented as flattening after 25 minutes because 27% of the cells were still present eight days later.

Case 4 —A woman, aged 35, who had never been transfused, was found to have anti Le^a in her serum during the course of her third pregnancy Four years later her serum reacted well in vitro at 37°C with cells from donors with "strong" Lewis antigens but poorly with cells from donors (such as H L) with "weak" Lewis antigens At this time, when the titre of anti Le^a was 1/1, she was injected with labelled Le(a+) cells (from donor H L as used in cases 2 and 3) During the 30 minutes after injection 65% of the cells were removed from the circulation (see fig 2), however, the remaining cells survived almost normally, with the result that three weeks after injection 23% of the total number injected were still present

Case 5 —A man, aged 70, admitted to hospital for trans urethral prostatectomy, had never previously been transfused In the course of selecting blood to hold in reserve during operation the patient's serum was found to agglutinate all samples of blood with which it was tested at room temperature Further investigation showed that the patient's serum contained an auto agglutinin acting weakly at room temperature, and an anti P agglutinin acting strongly at room temperature At 37°C the serum weakly agglutinated P positive cells and caused partial lysis of ficin treated P positive cells Fresh (but not heated) serum gave a weakly positive indirect anti globulin reaction with P positive cells (titre 1/2)

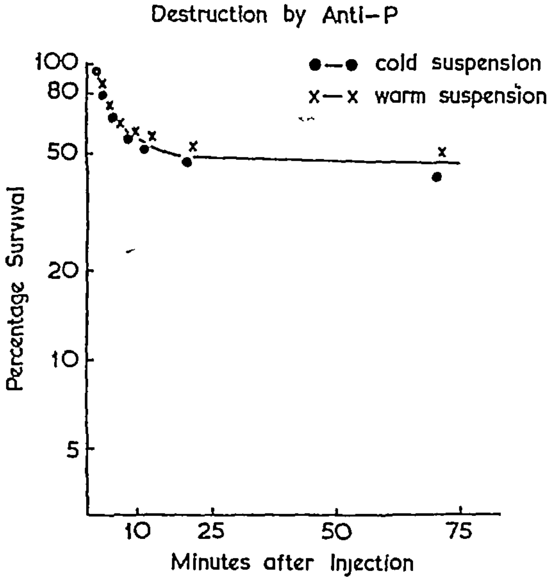

Fig 3—Survival of P positive cells in case 5 The cells injected as an ice-cold suspension were labelled with ^{32}P, those (from the same donor) injected as a warm suspension (39°C) were labelled with ^{51}Cr

The patient was transfused with P negative blood, and injections of labelled P positive cells were given On three separate occasions the pattern of elimination was essentially the same—namely, removal of about 50% of the injected cells in 10–15 minutes, followed by very much slower removal of the remainder For example, on one occasion the percentage of cells surviving 70 minutes after injection was 51% Next day the percentage survival was unchanged, after 9 days the number had fallen to 31%, and after 29 days to 17% Labelled P negative cells were found to survive normally

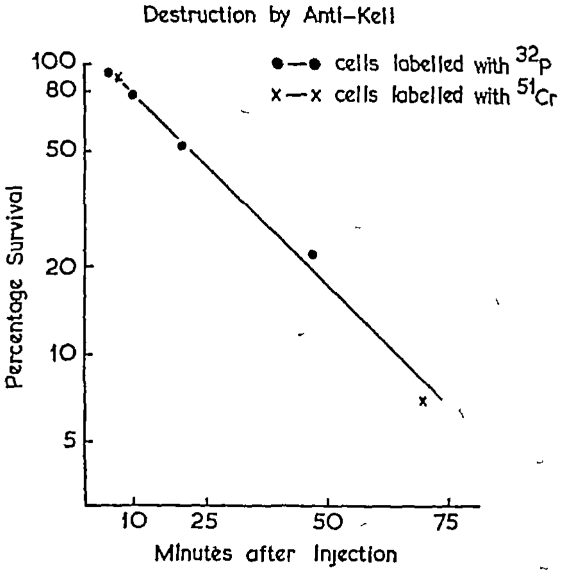

Fig 4—Survival of Kell positive cells in case 6 There was an interval of three days between the two injections, the titre of anti Kell was the same on both occasions, and the cells of the same donor were used

To discover whether the temperature of the suspension of P positive cells injected influenced their survival, the following experiment was made on two occasions The cells of a P positive donor were labelled with ^{32}P, suspended in ice cold saline solution, and kept in a bath at 0°C until injected Cells from the same donor were labelled with ^{51}Cr, suspended in warm saline solution, and kept in a bath at about 39°C until injected The warm suspension was rapidly injected into a vein, followed by a few ml of saline solution at 20°C, followed by the ice cold suspension The survival of the cells is illustrated in fig 3 Note that the cells injected at body temperature were eliminated just as rapidly during the first ten minutes as the cells injected as a cold suspension The same donor was used on both occasions, and close agreement was found between the results of the two tests—e g, 12 minutes after injection the results were as follows "warm" cells 56% and 57%, and "cold" cells 53% and 52% on the two occasions.

Constant Rate of Elimination with a Half-period of 20–30 Minutes

This mode of elimination was observed when Kell positive cells were injected into case 6, whose serum contained anti-Kell It was also observed when Rh positive cells were injected into two patients whose serum contained anti-Rh, one of these patients (case 1) is described in this section, the other (case 7) is described in a later section because initially she showed a different pattern of elimination

Case 6 —A woman with paroxysmal nocturnal hæmoglobinuria had been transfused many times, and her serum contained anti Kell The survival of Kell positive cells is illustrated in fig 4 Note that the number of surviving cells fitted a semilogarithmic plot, it appeared that there was a lag of about three minutes after injection before the cells

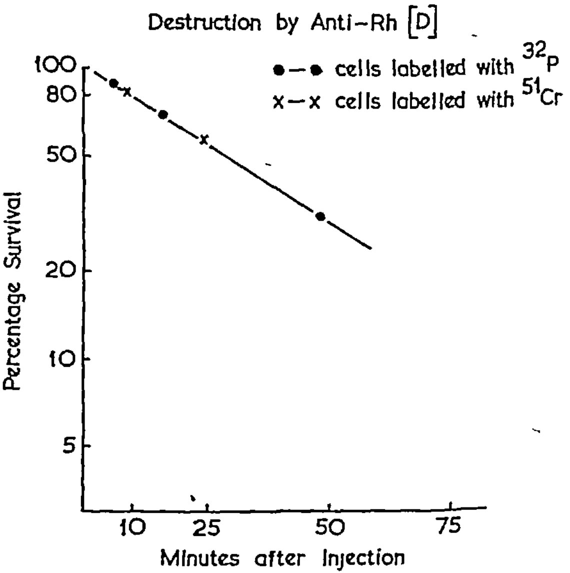

Fig 5—Survival of Rh-positive cells in case 1 The injections were given at an interval of two weeks, using red cells from the same donor On the first occasion the anti Rh titre was 1/64; on the second occasion it was 1/2000

started to disappear thereafter 50% were removed in 20 minutes. Kell positive cells were injected on two separate occasions, being labelled with ^{51}Cr the first time and with ^{32}P the second time three days later The results on the two occasions were essentially the same and the titre of anti Kell remained at 1/16 On the first occasion the number of injected cells decreased steadily over the 70 minutes following injection, only 7% being left at that time However next day 3-4% were still present; three days later they had all gone Kell negative cells survived normally in this patient

Case 1.—This was the patient already described above whose serum contained both anti Fy^a and anti Rh (—D) Rh positive (CDe/cDE) Fy(a—) cells were injected on two occasions, being labelled with ^{32}P the first time and with ^{51}Cr two weeks later The titre of Rh antibody rose considerably after the first injection, being 1/64 at the time of the first injection and 1/2000 at the time of the second injection. Despite this the rate of elimination was no more rapid on the second occasion (see fig 5) Note that the number of surviving cells, plotted on a logarithmic scale against time, fell upon a straight line; the time required for the removal of 50% of the cells was 28 minutes.

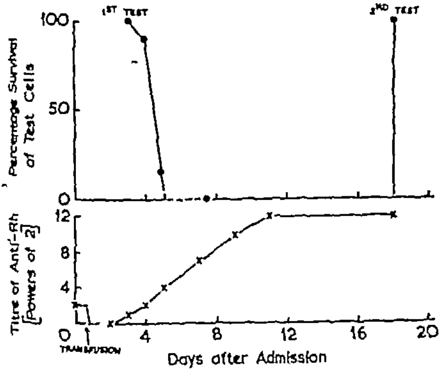

Fig. 6.—Changes in titre of anti-Rh and survival of labelled Rh-positive cells during 18 days following the transfusion of Rh-positive blood in case 7 The Rh-positive (CDe/CDe) cells injected three days after transfusion when the anti-Rh titre was 1/1 were eliminated relatively slowly (10% in 24 hours 90% in two days) The cells (from the same donor) injected 18 days after transfusion when the antibody titre was about 1/2000 were eliminated rapidly (half-period about 30 minutes)

Temporary Slowing of Rate of Elimination of Incompatible Cells, due to Adsorption of Antibody

After the transfusion of relatively large amounts of incompatible blood the antibody may all be adsorbed on to the incompatible cells In these circumstances the rate of elimination of a further transfusion of incompatible cells may be relatively slow If there is an immune response and the amount of antibody increases considerably, the incompatible cells may be rapidly eliminated, as in the following case

Case 7.—A woman, aged 58 with carcinoma of the rectum and abdominal metastases, had been transfused with Rh positive blood a year previously During an emergency operation she was transfused with 500 ml of Rh positive blood under the impression that she was Rh positive a 30-minute cross matching test in albumin had not revealed incompatibility Further testing showed that the patient was Rh negative and that her serum contained Rh antibody (indirect anti globulin test) Three days later her blood still contained circulating Rh positive red cells. This was demonstrated in two ways: (1) by showing that clumps of M cells were present, the donor being type M and the recipient type N; and (2) by showing that a small proportion of the patient s cells were strongly agglutinated by an anti globulin serum. Three days after the transfusion of 500 ml of Rh positive blood there was very little free anti Rh in the patient s serum (titre 1/1); a test injection of Rh positive cells (CDe/CDe) was given There was no change whatever in the count of the injected cells during the two and a half hours following the injection next day 90% were still present but on the following day only 14% were present (see fig 6) A test made two days later showed no trace of surviving cells This rapid decrease in the number of surviving cells coincided with the rapid increase in the amount of Rh antibody in the patient s serum. Fifteen days after the first test a second injection of Rh positive cells from the same donor was given, when the titre of Rh antibody was very high (1/2000) The cells were rapidly eliminated, 50% being removed in about 30 minutes the estimates fitted a semilogarithmic plot

Constant Rate of Elimination with a Half-period of Several Days

In some instances the amount of antibody or its character appears to be inadequate to bring about the rapid elimination of incompatible cells In the following case despite the presence in the patient's serum of anti-c in a titre of 1/16 c-positive cells were eliminated relatively slowly (50% in 5–7 days)

Case 8.—A woman aged 41 was admitted after having had a considerable hæmatemesis presumably from an acute gastric erosion. She had had three pregnancies six months previously she had been transfused with blood from two donors. Preliminary matching tests showed that her serum contained anti-c. She was transfused with blood from three Rh positive donors without any untoward reaction but rechecking showed that one of the donors was c-positive Testing of the patient s blood eight hours after transfusion showed that most, or all of these cells were present (positive direct anti-globulin test) The anti-c which had been easily demonstrable in the patient s serum before transfusion (titre 1/16) was now extremely weak (titre 1/2) An injection of labelled c positive cells (cde/cde) was given the survival of these cells is illustrated in fig 7 Note that for the first 14 days the numbers of surviving cells, when plotted on a semi logarithmic scale against time fall upon a straight line 50% of the cells being eliminated in just over seven days. After 14 days the slope of elimination became a little steeper perhaps because the patient had a mild immune response There was no evidence of any further bleeding during the period of the observations

Thirty-six days after she had received the transfusion of incompatible blood, and at a time when her circulation contained no trace of surviving c positive cells she was given a further test injection of c positive cells from the same donor (cde/cde) whose cells had been injected previously The survival of these cells is also shown in fig 7 Note that

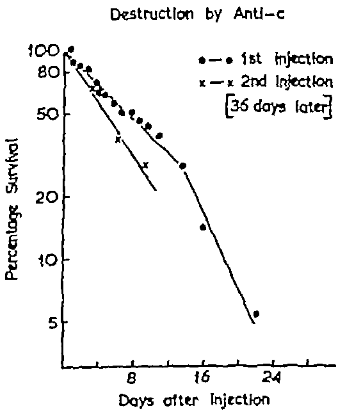

Fig. 7.—Survival of c-positive cells in case 7 Note that the time scale is in days. The first injection of labelled cells was given 12 hours after the patient had been transfused with 500 ml. of c-positive blood The second injection was given when all the transfused c-positive cells had been eliminated.

elimination was only slightly more rapid than on the first occasion, 50% of the cells being eliminated in about five days The titre of anti-c at the time of the first injection was 1/2, at the time of the second injection it was 1/8–1/16

Elimination Unaffected by Non-specific Cold Agglutinins

There is a good deal of evidence that when cold agglutinins, capable of reacting at room temperature but incapable of reacting at 37°C, are present in the serum they do not influence the survival of transfused red cells. The following case provides further evidence

Case 9 —A young man with acute leukæmia had been transfused eight times during the previous four months His serum agglutinated all red cells except his own However, the reactions took place only at room-temperature and not at 37°C The indirect anti globulin test was negative The red cells of a donor whose cells were strongly agglutinated by the patient's serum at room temperature were injected as a cold suspension, their survival was within normal limits for the three days during which it was followed

Discussion

Radioactive phosphorus and radioactive chromium appear to be equally satisfactory red-cell labels for investigations lasting only an hour However, ^{51}Cr is evidently more suitable if the survival of the red cells is to be followed longer There is evidence that, provided the dose of chromium does not exceed about 25 µg per ml. of red cells, their survival is unaffected (Donohue et al 1955) In the present work the dosage never exceeded 10 µg per ml and was sometimes as low as 2 µg per ml of red cells For this particular type of work it is evidently a great advantage to use ^{51}Cr of very high specific activity, such as that produced by the Szilard Chalmers reaction (see Mollison and Veall 1955)

The present observations provide further evidence that, when ^{51}Cr-labelled red cells are broken down, the chromium is not re utilised by other cells (Ebaugh et al 1953) For example, in one case on the day following the injection of labelled incompatible cells no radioactivity was detected in a sample of red cells taken from the patient, the plasma contained about 1% of the injected radioactivity When ^{32}P labelled red cells were rapidly destroyed, a small fraction of the ^{32}P appeared to label other red cells, with the result that about 1–3% of the injected activity remained in the blood

In all the cases described here the volume of incompatible cells injected was about 1 ml, no untoward symptoms were noted, even when all the injected cells were destroyed within ten minutes

There appear to be two main patterns of elimination of incompatible cells The characteristics of the first type of elimination are as follows after injection there is a brief lag-phase, lasting about two and a half minutes, before destruction begins Then a large proportion of the cells undergo rapid destruction, presumably by intravascular lysis The proportion of cells destroyed rapidly varies from 50 to 100% Case 2 represents one extreme, 90% of the injected cells having been destroyed in five minutes At the other extreme lie cases 4 and 5, in which 50% of the cells were destroyed in about 15 minutes and the remainder survived for three weeks or more (see table) It must be concluded that within a population of red cells susceptibility to destruction by the antibodies anti-Le^a and anti-P varies widely Apparently, however, relative insensitivity may be overcome if the antibody is strong enough, this is well shown by fig 2

O'Brien et al (1954) report in dogs findings which are similar in some respects to those reported here Thus, in dogs whose serum contains canine anti A, dog A_1 cells are very rapidly eliminated, but, when A_2 cells are transfused, only about 50% are rapidly destroyed, the remainder being slowly eliminated over one or two months

In the second main pattern of destruction, illustrated in figs 4 and 5, the red cells are removed from the circulation with a half-period of 20–30 minutes, and the points appear to fit a semilogarithmic plot Dr N Veall (personal communication) suggests that this may represent the time required for half the cells to pass through the spleen He points out that, if 3% of the circulating blood passes through the spleen each minute, and if the blood in passing is cleared completely of incompatible cells, it will take about 25 minutes to remove half the incompatible cells from the circulation

DESTRUCTION OF RED CELLS

Case no	Specific antibody	Time taken for destruction of	
		50 % of cells (min)	90 % of cells
1	anti Fy^a	5	20 min.
2*	anti Le^a	1¼	5 min
3*	anti Le^a	5½	More than 24 hr
4*	anti Le^a	16	More than 3 wk
5	anti P	15	More than 4 wk.

* The same donor (H L) was used in these three cases
The time taken for destruction was measured from a point 2½ minutes after injection (see text)

When the Rh antibody titre is as high as 1/2000, destruction is no more rapid than when it is as low as 1/64 (case 1, see fig 5) It must be supposed that, in this type of destruction of red cells, provided the red cells are "saturated" with antibody, the rate of elimination cannot be raised further by increasing the amount of antibody However, when the titre of Rh antibody is low (e g, 1/2) the red cells may be destroyed considerably more slowly, as in case 7 (see fig 6)

The relatively slow destruction of c positive cells in case 8 was rather surprising Before the transfusion of 500 ml of c-positive blood the titre of anti-c was 1/16, the slow elimination of the incompatible cells of this blood, and of the 1 ml of labelled cells injected 12 hours later, was thought to be due to temporary absorption of antibody, the titre of free antibody having fallen to 1/2 However, 36 days after the transfusion, when the titre of anti-c had risen again to 1/16, 1 ml of c-positive cells was eliminated almost equally slowly

Although in this last patient (case 8) the elimination of incompatible cells was scarcely more rapid when 1 ml was injected than when a whole bottle of blood was transfused, it would be unwise to conclude that the volume of injected cells normally has little influence on the rate of elimination Indeed, experimental work in dogs has shown that, if two incompatible transfusions are given in succession, the second lot of red cells is less rapidly destroyed, evidently because the amount of antibody in the recipient's circulation has been reduced (Christian et al 1951) In practice the fact that a small volume of incompatible cells may be more rapidly eliminated than a large volume does not impair the value of the test proposed here The prime object of the test is to obtain evidence for or against the compatibility of the cells of a given donor, and for this it is only necessary to discover whether or not there is any departure from the normal rate of elimination

When incompatibility is due to antibodies which are hæmolytic in vitro, it is to be expected that intravascular lysis will occur in vivo Anti Le^a and anti-P have been reported as being lytic in vitro (Andresen 1950, Rosenfield and Vogel 1951, Moureau 1945) The anti-Le^a and anti P sera encountered in the present work would hæmolyse enzyme-treated cells but not untreated cells in vitro In vivo, both these antibodies very rapidly eliminated a large proportion of the injected cells In case 2 the transfusion of Le(a+) blood was followed by hæmoglobinuria, as in a previously reported case of "suspected incompatibility due to anti Le^a" (Brendemoen and Aas 1952)

The very rapid elimination of labelled cells by anti Fy^a was unexpected, although hæmoglobinuria has been reported in a case of incompatibility due to this antibody (Wiener 1954)

If it is true that anti Rh and anti Kell normally cause extravascular destruction as suggested by the present observations, it might seem that these antibodies should not cause hæmoglobinæmia Intravascular hæmolysis has been reported after the transfusion of Rh positive blood to patients with Rh antibody in their serum (Vogel et al 1943) and after the transfusion of Kell positive blood to a patient with anti Kell (Young 1954) In these cases it must be supposed either that the antibody has become capable of bringing about intravascular hæmolysis or that when extravascular destruction is very rapid, there is some spill over of the hæmoglobin into the plasma

In all the cases reported here in which injected red cells were destroyed at an increased rate the incompatibility could have been predicted from the results of the anti globulin test—i e the patient's serum at 37°C, sensitised the donor's cells to an anti globulin serum However, the reactions were much stronger with some anti globulin sera than with others This applied particularly to cells sensitised with anti Le^a and anti P As reported here, these antibodies are not gamma globulins and their detection depends on the presence of anti beta globulin in the anti globulin sera Some anti globulin sera contain relatively little anti beta globulin and are unsuitable for detecting these particular blood group antibodies (Crawford et al 1955)

It should be emphasised that the presence of anti Le and anti P could be detected by the anti globulin test only if the patient's fresh serum was used It follows that in cross-matching tests if a fresh sample of serum is not available fresh normal serum should be added to the serum-cell mixtures Plasma should not be used anticoagulants being anticomplementary

Dacie (1950) has shown that the incomplete cold antibody found in normal serum and the incomplete antibody found in the cold type of acquired hæmolytic anæmia are adsorbed on to red cells only in the presence of complement moreover red cells sensitised with these antibodies react with anti globulin sera to which gamma globulin has been added The present observations show that in these respects anti Le^a and anti P are similar

Summary

The survival of transfused cells can be estimated by using volumes of cells as small as 1 ml ^{32}P is suitable as a label when the survival is to be followed for an hour or so, but ^{51}Cr must be used when survival is to be followed for days or weeks

When incompatible red cells were injected their elimination followed one of two main patterns

(1) In the first pattern 50–100% of the cells were destroyed within ten minutes; cells surviving at the end of this period were much more slowly destroyed This pattern of elimination was seen when cells were injected into patients whose serum contained anti Fy^a anti Le^a or anti P

(2) In the second pattern the cells were eliminated at a steady rate with a half period of 20–30 minutes. This pattern was seen when cells were injected into patients whose serum contained anti Rh or anti Kell.

It is suggested that measurement of the rate of elimination of small volumes of injected red cells may be a useful biological test in cases in which the interpretation of compatibility tests in vitro is difficult

In all cases in which red cells were rapidly destroyed in vivo the indirect anti globulin test was positive in vitro However in cases where the serum contained anti Le^a or anti P the cells were sensitised only if incubated with fresh serum Moreover in these cases it was shown that the reaction of the sensitised cells with anti globulin serum depended not on anti gamma globulin but upon anti beta globulin Some anti globulin sera were unsuitable for the detection of these antibodies.

We are indebted to Dr Eloise R Giblett for her assistance in these investigations Dr J V Dacie and Dr J H Crookston for calling our attention to many of these cases; Prof. J McMichael Dr C L Cope and Prof J M Browne for permission to investigate patients under their care Dr J D James Dr P B Booth, and Dr G Plaut, of the North London Blood Transfusion Centre for their help on numerous occasions in collecting blood from donors; and Dr G H. Grant for serum from a patient with agammaglobulinæmia

REFERENCES

Andresen, P H (1950) Personal communication.
Brendemoen O J Aas K. (1952) *Acta med scand* 141 458
Chaplin H jun. (1954) *J Physiol* 123 22.
Christian R. M., Stewart, W B Yuile C L. Ervin D M. Young L E (1951) *Blood* 6 142
Crawford H Cutbush, M. Mollison P L (1955) *Brit. J Hæmatol* (in the press)
Dacie J V (1950) *Nature Lond* 166 36
Dodge O G (1953) *J clin Path.* 5, 102
Donohue, D M. Motulsky A. G Giblett, E R. Pirzio-Biroli, G Viranuvatti V Finch C A. (1955) *Brit J Hæmatol.* (in the press)
Ebaugh F G jun Emerson, C P Ross J F (1953) *J clin. Invest* 32, 1260
Mollison P L. (1951) Blood Transfusion in Clinical Medicine Oxford p 301
— Veall N (1955) *Brit J Hæmatol* 1 62
Moureau P (1945) *Rev belge Sci Med* 16 258
O Brien W A Swisher, S N Young L E (1954) *Trans Ass Amer Physns* 67, 124
Reeve E B Veall, N (1949) *J Physiol.* 108 12
Rosenfield, R. E., Vogel, P (1951) *Trans. N Y Acad Sci* 13 213
Vogel, P Rosenthal, N Levine P (1943) *Amer J clin. Path.* 13 1
Wiener, A. S (1954) *N Y St J Med* 54, 3071
— Silverman I J Aronson W (1942) *Amer J clin. Path.* 12 241
Young L E. (1954) *Amer J Med.* 16 878

INCREASED EXCRETION OF ALDOSTERONE IMMEDIATELY AFTER OPERATION

J G LLAURADO
M.D Barcelona
LECTURER IN EXPERIMENTAL SURGERY IN THE UNIVERSITY OF OTAGO DUNEDIN NEW ZEALAND

> "The urine of man is one of the animal matters that have been the most examined by chemists and of which the examination has at the same time furnished the most singular discoveries to chemistry and the most useful application to physiology as well as the art of healing (De Fourcroy 1801)

IT is well known that surgical trauma is followed by a positive sodium balance and a negative potassium balance. Several hypotheses have been formulated (Wilkinson et al 1950 Winfield et al 1951 Schilling et al. 1953 Le Quesne 1953) to explain the increased excretion of K^+ Some workers have postulated that the adrenal cortex plays the chief rôle in this alteration of electrolyte metabolism but hitherto evidence for this hypothesis has been lacking In recent years several reports have been published of the occurrence of a sodium retaining factor in some human urine but neither the salt-conserving action of this factor nor indeed the rôle of the adrenal cortex in controlling electrolyte balance in healthy people can be explained by the activity of deoxycortone (Luetscher et al 1952) which until recently was the only steroid known to possess such sodium retaining properties in high degree The discovery by Grundy et al (1952) of a new hormone of the adrenal cortex now called aldosterone which has the ability to increase greatly both Na^+ retention and K^+ excretion by the kidney the subsequent isolation of this hormone (Simpson et al 1953) and the determination of its chemical structure (Simpson et al 1954) have given a new impetus to the investigation of clinical disturbances associated with Na^+ retention and increased K^+ excretion

In a previous paper (Cope and Llaurado 1954) it was reported that aldosterone (electrocortin) was present in large amounts in the urine of a patient suffering K^+ loss (Evans and Milne 1954) Since the communication by Conn (1954) it seems clear that the case was one of primary aldosteronism elimination was only slightly more rapid than on the first occasion, 50% of the cells being eliminated in about five days The titre of anti-c at the time of the first injection was 1/2, at the time of the second injection it was 1/8–1/16

Elimination Unaffected by Non-specific Cold Agglutinins

There is a good deal of evidence that when cold agglutinins, capable of reacting at room temperature but incapable of reacting at 37°C, are present in the serum they do not influence the survival of transfused red cells The *following case provides further evidence*

Case 9 —A young man with acute leukæmia had been transfused eight times during the previous four months His serum agglutinated all red cells except his own However, the reactions took place only at room temperature and not at 37°C The indirect anti globulin test was negative The red cells of a donor whose cells were strongly agglutinated by the patient's serum at room temperature were injected as a cold suspension, their survival was within normal limits for the three days during which it was followed

Discussion

Radioactive phosphorus and radioactive chromium appear to be equally satisfactory red-cell labels for investigations lasting only an hour However, ^{51}Cr is evidently more suitable if the survival of the red cells is to be followed longer There is evidence that, provided the dose of chromium does not exceed about 25 µg per ml. of red cells, their survival is unaffected (Donohue et al 1955) In the present work the dosage never exceeded 10 µg per ml and was sometimes as low as 2 µg per ml of red cells For this particular type of work it is evidently a great advantage to use ^{51}Cr of very high specific activity, such as that produced by the Szilard Chalmers reaction (see Mollison and Veall 1955)

The present observations provide further evidence that, when ^{51}Cr-labelled red cells are broken down, the chromium is not re utilised by other cells (Ebaugh et al 1953) For example, in one case on the day following the injection of labelled incompatible cells no radioactivity was detected in a sample of red cells taken from the patient, the plasma contained about 1% of the injected radioactivity When ^{32}P labelled red cells were rapidly destroyed, a small fraction of the ^{32}P appeared to label other red cells, with the result that about 1–3% of the injected activity remained in the blood

In all the cases described here the volume of incompatible cells injected was about 1 ml, no untoward symptoms were noted, even when all the injected cells were destroyed within ten minutes

There appear to be two main patterns of elimination of incompatible cells The characteristics of the first type of elimination are as follows after injection there is a brief lag phase, lasting about two and a half minutes, before destruction begins Then a large proportion of the cells undergo rapid destruction, presumably by intravascular lysis The proportion of cells destroyed rapidly varies from 50 to 100% Case 2 represents one extreme, 90% of the injected cells having been destroyed in five minutes At the other extreme lie cases 4 and 5, in which 50% of the cells were destroyed in about 15 minutes and the remainder survived for three weeks or more (see table) It must be concluded that within a population of red cells susceptibility to destruction by the antibodies anti-Le^a and anti-P varies widely Apparently, however, relative insensitivity may be overcome if the antibody is strong enough, this is well shown by fig 2

O'Brien et al (1954) report in dogs findings which are similar in some respects to those reported here Thus, in dogs whose serum contains canine anti A, dog A$_1$ cells are very rapidly eliminated, but, when A$_2$ cells are transfused, only about 50% are rapidly destroyed, the remainder being slowly eliminated over one or two months

In the second main pattern of destruction, illustrated in figs 4 and 5, the red cells are removed from the circulation with a half-period of 20–30 minutes, and the points appear to fit a semilogarithmic plot Dr N Veall (personal communication) suggests that this may represent the time required for half the cells to pass through the spleen He points out that, if 3% of the circulating blood passes through the spleen each minute, and if the blood in passing is cleared completely of incompatible cells, it will take about 25 minutes to remove half the incompatible cells from the circulation

DESTRUCTION OF RED CELLS

Case no	Specific antibody	Time taken for destruction of —	
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1	anti Fy^a	5	20 min
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3*	anti Le^a	$5\frac{1}{2}$	More than 24 hr
4*	anti Le^a	16	More than 3 wk
5	anti P	15	More than 4 wk

* The same donor (H L) was used in these three cases

The time taken for destruction was measured from a point $2\frac{1}{2}$ minutes after injection (see text)

When the Rh antibody titre is as high as 1/2000, destruction is no more rapid than when it is as low as 1/64 (case 1, see fig 5) It must be supposed that, in this type of destruction of red cells, provided the red cells are "saturated" with antibody, the rate of elimination cannot be raised further by increasing the amount of antibody However, when the titre of Rh antibody is low (e g, 1/2) the red cells may be destroyed considerably more slowly, as in case 7 (see fig 6)

The relatively slow destruction of c positive cells in case 8 was rather surprising Before the transfusion of 500 ml of c-positive blood the titre of anti-c was 1/16, the slow elimination of the incompatible cells of this blood, and of the 1 ml of labelled cells injected 12 hours later, was thought to be due to temporary absorption of antibody, the titre of free antibody having fallen to 1/2 However, 36 days after the transfusion, when the titre of anti c had risen again to 1/16, 1 ml of c positive cells was eliminated almost equally slowly

Although in this last patient (case 8) the elimination of incompatible cells was scarcely more rapid when 1 ml was injected than when a whole bottle of blood was transfused, it would be unwise to conclude that the volume of injected cells normally has little influence on the rate of elimination Indeed, experimental work in dogs has shown that, if two incompatible transfusions are given in succession, the second lot of red cells is less rapidly destroyed, evidently because the amount of antibody in the recipient's circulation has been reduced (Christian et al 1951) In practice the fact that a small volume of incompatible cells may be more rapidly eliminated than a large volume does not impair the value of the test proposed here The prime object of the test is to obtain evidence for or against the compatibility of the cells of a given donor, and for this it is only necessary to discover whether or not there is any departure from the normal rate of elimination

When incompatibility is due to antibodies which are hæmolytic in vitro, it is to be expected that intravascular lysis will occur in vivo Anti Le^a and anti-P have been reported as being lytic in vitro (Andresen 1950, Rosenfield and Vogel 1951, Moureau 1945) The anti Le^a and anti P sera encountered in the present work would hæmolyse enzyme treated cells but not untreated cells in vitro In vivo, both these antibodies very rapidly eliminated a large proportion of the injected cells In case 2 the transfusion of Le(a+) blood was followed by hæmoglobinuria, as in a previously reported case of "suspected incompatibility due to anti-Le^a" (Brendemoen and Aas 1952)

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If it is true that anti Rh and anti Kell normally cause extravascular destruction, as suggested by the present observations, it might seem that these antibodies should not cause hæmoglobinæmia. Intravascular hæmolysis has been reported after the transfusion of Rh positive blood to patients with Rh antibody in their serum (Vogel et al 1943) and after the transfusion of Kell positive blood to a patient with anti Kell (Young 1954). *In these cases it must be supposed either that the* antibody has become capable of bringing about intravascular hæmolysis or that when extravascular destruction is very rapid there is some spill over of the hæmoglobin into the plasma.

In all the cases reported here in which injected red cells were destroyed at an increased rate the incompatibility could have been predicted from the results of the anti globulin test—i.e. the patient's serum, at 37°C sensitised the donor's cells to an anti globulin serum. However the reactions were much stronger with some anti globulin sera than with others. This applied particularly to cells sensitised with anti Le^a and anti P. As reported here, these antibodies are not gamma globulins and their detection depends on the presence of anti beta globulin in the anti globulin sera. Some anti globulin sera contain relatively little anti beta globulin and are unsuitable for detecting these particular blood group antibodies (Crawford et al 1955).

It should be emphasised that the presence of anti Le^a and anti P could be detected by the anti globulin test only if the patient's fresh serum was used. It follows that in cross matching tests if a fresh sample of serum is not available, fresh normal serum should be added to the serum-cell mixtures. Plasma should not be used, anticoagulants being anticomplementary.

Dacie (1950) has shown that the incomplete cold antibody found in normal serum and the incomplete antibody found in the cold type of acquired hæmolytic anæmia are adsorbed on to red cells only in the presence of complement; moreover red cells sensitised with these antibodies react with anti globulin sera to which gamma globulin has been added. The present observations show that in these respects anti Le^a and anti P are similar.

Summary

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It is suggested that measurement of the rate of elimination of small volumes of injected red cells may be a useful biological test in cases in which the interpretation of compatibility tests in vitro is difficult.

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REFERENCES

Andresen, P H (1950) Personal communication.
Brendemoen, O J, Aas K (1952) *Acta med scand* 141 458
Chaplin, H jun (1954) *J Physiol* 123 22
Christian R M, Stewart, W B, Yuile C L, Ervin D M, Young, L E (1951) *Blood* 6 142
Crawford H, Cutbush, M, Mollison P L (1955) *Brit J Hæmatol.* (in the press)
Dacie J V (1950) *Nature, Lond* 166 36
Dodge O G (1952) *J clin Path* 5, 102
Donohue D M, Motulsky A G, Giblett, E R, Pirzio-Biroli, G, Viranuvatti V, Finch C A (1955) *Brit J Hæmatol.* (in the press)
Ebaugh F G jun, Emerson, C P, Ross J F (1953) *J clin Invest* 32, 1260
Mollison P L (1951) Blood Transfusion in Clinical Medicine Oxford p 301
— Veall, N (1955) *Brit J Hæmatol* 1 62
Moureau P (1945) *Rev belge Sci Med* 16 258
O'Brien W A, Swisher, S N, Young L E (1954) *Trans Ass Amer Phycns* 67, 144
Reeve, E B, Veall, N (1949) *J Physiol* 108 12
Rosenfield, R E, Vogel P (1951) *Trans N Y Acad Sci* 13 213
Vogel, P, Rosenthal N, Levine P (1943) *Amer J clin Path* 13 1
Wiener, A S (1954) *N Y St J Med* 54, 3071
— Silverman, I J, Aronson W (1942) *Amer J clin Path* 12 241
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> The urine of man is one of the animal matters that have been the most examined by chemists and of which the examination has at the same time furnished the most singular discoveries to chemistry and the most useful application to physiology as well as the art of healing. (De Fourcroy 1801)

It is well known that surgical trauma is followed by a positive sodium balance and a negative potassium balance. Several hypotheses have been formulated (Wilkinson et al 1950 Winfield et al 1951 Schilling et al 1953 Le Quesne 1953) to explain the increased excretion of K$^+$. Some workers have postulated that the adrenal cortex plays the chief rôle in this alteration of electrolyte metabolism, but hitherto evidence for this hypothesis has been lacking. In recent years several reports have been published of the occurrence of a sodium retaining factor in some human urine but neither the salt-conserving action of this factor nor indeed the rôle of the adrenal cortex in controlling electrolyte balance in healthy people can be explained by the activity of deoxycortone (Luetscher et al 1952) which until recently was the only steroid known to possess such sodium retaining properties in high degree. The discovery by Grundy et al (1952) of a new hormone of the adrenal cortex now called aldosterone which has the ability to increase greatly both Na$^+$ retention and K$^+$ excretion by the kidney the subsequent isolation of this hormone (Simpson et al 1953) and the determination of its chemical structure (Simpson et al 1954) have given a new impetus to the investigation of clinical disturbances associated with Na$^+$ retention and increased K$^+$ excretion.

In a previous paper (Cope and Llaurado 1954) it was reported that aldosterone (electrocortin) was present in large amounts in the urine of a patient suffering K$^+$ loss (Evans and Milne 1954). Since the communication by Conn (1954) it seems clear that the case was one of primary aldosteronism.

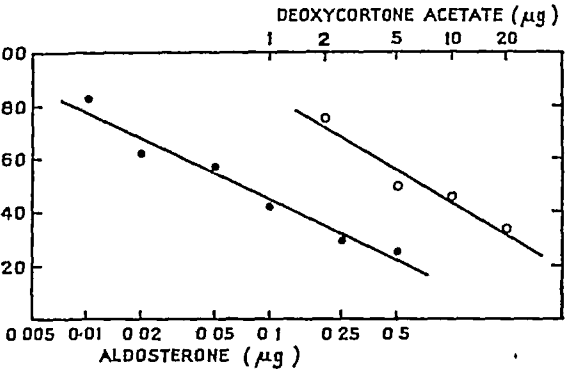

Fig 1—Effect of aldosterone and deoxycortone acetate on Na^+/K^+ ratio percentage of control Note linear relationship between log-dose and fall of Na^+/K^+ ratio percentage Aldosterone proves to be 100 times as strong as deoxycortone.

In the light of these facts it seemed important to determine whether the well-known phenomenon of K^+ loss following surgical trauma could also be explained by increased secretion of the electrolyte-regulating corticoid (presumably aldosterone) In the work presented here a search was made for this corticoid in the urine of patients before and at various stages after surgical operation This paper deals only with the results obtained before and immediately after operation A brief preliminary account of the results has been published (Llaurado 1954)

Methods

The methods of extracting aldosterone from urine and of estimating it by bio assay have been fully described previously (Cope and Llaurado 1954) The only difference introduced here is that ordinary Na^+ and K^+ have been used as loading injections to the rats, instead of radioactive $^{24}Na^+$ and $^{42}K^+$, since it has been statistically shown (Cope and Llaurado 1955) that the same degree of accuracy and sensitivity of the method can be reached by using non radioactive materials In the experiments reported here adult patients were chosen to include members of either sex with various clinical conditions and submitted to operations of various grades of severity Twenty four hour samples of urine were collected without preservative, the first before operation, and the second during the twenty four hours immediately after operation When there was anuria for the twenty four hours after operation, the next twenty-four hour specimen was taken as immediate postoperative collection No distinction was made between urine passed spontaneously by the patient and urine obtained by catheter

For injections into rats the dry extract was dissolved in 20% ethanol in water, the volume being so chosen that the dose to be injected (three hours *) into each rat was contained in 0 1 ml of solution.

The sodium and potassium were estimated in human urine in the aqueous phase of urine after extraction This procedure was adopted because the small amount of urine passed by the postoperative patient in twenty four hours made it advisable not to reduce the amount of urine before steroid extraction Preliminary experiments showed that the amount of steroid solvent left in the urine does not produce any interference at the flame, the results being the same as those obtained with urine before any manipulation An 'Eel' flame photometer was used for all Na^+ and K^+ estimations

Results

ASSAYS WITH CRYSTALLINE ALDOSTERONE

To obtain a standard of reference, bio assays were made with known quantities of pure crystalline aldosterone, kindly made available by Prof T Reichstein of Basle A linear relationship (fig 1) was found between percentage of Na^+/K^+ ratio response and log dose of aldosterone in a range from 0 01 μg to 0 5 μg Statistical data are tabulated in table I The new steroid proved to be 100 times as active (fig 1) as deoxycortone acetate (effective dose 2–20 μg) when assayed by the same method, and this result is in complete agreement with the earlier data published by Simpson and Tait (1953)

Some workers (Desaulles et al 1953, Swingle et al 1954) have suggested that aldosterone differs both quantitatively and qualitatively from deoxycortone acetate in the way in which it acts on electrolyte metabolism The present results, however, do not support this assertion, because the difference of slopes of regression lines of aldosterone and deoxycortone acetate do not differ significantly when analysed statistically, and favour the view that they are only quantitatively different.

Stability of Aldosterone in water alcohol solutions —Swingle et al (1954) reported that aldosterone retains the same biological activity when kept in 95% ethanol solution. In the present experiments a solution of aldosterone in 20% ethanol in water retained complete biological activity after being kept six weeks in the refrigerator

Recovery of aldosterone from human urine —Aldosterone was added to pooled human urine, the usual method of extraction was used, and the results were compared with the same volume of analogous urine as a blank An average recovery of 20% was obtained as estimated by its biological activity This percentage of recovery is about the same as that obtained when a commercially available adrenal cortical extract ('Eucortone') was added to human urine and assayed by the same method (Cope and Llaurado 1954) Very similar values for aldosterone recovery are reported by Mills (1954)

TABLE I—PARAMETERS OF REGRESSION LINES OF ALDOSTERONE AND DEOXYCORTONE ASSAYS

Parameter	Aldosterone	Deoxycortone
Slope = $\lvert b \rvert$	32 95	39 30
S D.L *	4 69	5 59
S E $_b$†	3 26	7 55
$L = \frac{1}{\lambda} = \frac{\lvert b \rvert}{S D L}$	6 90	7 04
r (coefficient of correlation)	–0 98	–0 96
No of rats used	68 (and 25 controls)	57 (and 43 controls)

$$* S D L = \sqrt{\frac{\Sigma (y - y \text{ calc })^2}{N-2}} = \text{standard deviation about the line}$$

$$† S E_b = \frac{S D L}{\sqrt{\Sigma (x - \bar{x})^2}} = \text{standard error of the slope}$$

$$x = \log X \text{ (dose assayed)}$$

ASSAYS WITH EXTRACTS OF URINE

Six patients have been studied so far Some activity was found in the urine of some patients on the day before operation, but others showed none From the point of view of adrenal cortex activity these patients before operation can be considered as "normal," and the finding of activity in these conditions agrees with previous results reported by Chart and Shipley (1953), Cope and Llaurado (1954), Luetscher et al (1954), and Venning et al (1954)

The extracts from urine obtained after operation invariably showed an increased sodium-retaining activity compared with the level before operation The activity levels before and after operation are shown in table II The difference between preoperative and postoperative activity is statistically highly significant ($P < 0\ 001$, determined by Student's t test)

Table II shows also the twenty-four-hour output expressed as micrograms of aldosterone after operation, calculated from the regression line (fig 1) and corrected for percentage of extraction recovery The results range from 0 14 μg to 2 70 μg daily of aldosterone excretion with an average output of 1 11 μg daily

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[*] A three-hour dose is one-eighth of the extract obtained from a twenty four hour specimen of urine

TABLE II—COMPARATIVE DATA OF PATIENTS STUDIED BEFORE AND AFTER OPERATION

(Values under 100 indicate aldosterone activity in assayed urine) *

Case no.	Sex	Diagnosis	Operation	Aldosterone activity		24 hour output equivalent in µg. of aldosterone †		Volume of 24 hour urine (ml.)		Urine Na+ (m eq. per litre)		Urine K+ (m eq. per litre)	
				Preoperative	Postoperative	Preop	Postop	Preop	Postop	Preop	Postop	Preop	Postop
1	F	Biliary lithiasis	Cholecystectomy	101.7 ± 28.4	71.[illegible] ± 20.3		0.50	520	190	‡	‡	‡	‡
2	F	Inguinal hernia	Herniorrhaphy	110.0 ± 30.4	73.5 ± 24.1		0.43	980	190	‡	40.0	‡	200.0
3	M	Pulmonary tuberculosis	Thoracoplasty	78.8 ± 31.0	52.3 ± 1[illegible]	0.30	2.28	1300	270	111.3	79.4	48.3	124.0
4	F	Pulmonary tuberculosis	Lobectomy	99.0 ± 22.1	70.0 ± 16.0		0.64	1890	240	30.4	23.0	19.6	82.0
5	M	(?) Lung cancer	Lobectomy	96.6 ± 1[illegible].0	92.5 ± 17.0		0.14	1380	275	50.0	46.0	25.0	110.4
6	M	Œsophageal cancer	Œsophagojejunostomy	77.0 ± 18.2	50.1 ± 11.3	0.41	2.70	970	780	34.0	10.0	33.0	104.0

* Mean ± standard error.—S.E. calculated as follows

$$S.E. = \left[\frac{\frac{s_c}{\sqrt{n_c}}\,100}{m_c} + \frac{\frac{s_x}{\sqrt{n_x}}\,100}{m_x}\right]\frac{\frac{100\,m_x}{m_c}}{100}; \quad \text{where:}$$

$$\left.\begin{array}{l} s_c = \text{S.D. of control set}\\ s_x = \text{S.D. of unknown set}\end{array}\right\} = \sqrt{\Sigma\frac{(x-n)^2}{n}}$$

n_c = no. of rats in control set

n_x = no. of rats in unknown set

m_c = mean of control set

m_x = mean of unknown set

† Calculated from regression line and corrected for percentage of extraction recovery—values corresponding to aldosterone activity over 95% have not been calculated.

‡ Not estimated.

The activity shown by the extracts was quite independent of the total twenty-four-hour volume of urine (table II), this fact confirming the observation reported by Luetscher and Johnson (1954).

It was also found that the urinary Na^+/K^+ ratio in patients before operation was greater than 1, but that after operation it was very much less than 1. If the values obtained in the bio-assay and the Na^+/K^+ ratio of the patient's urine are plotted in the same graph (fig. 2), the diagrams which result show remarkable similarity. Great importance is attached to this fact because the activity of the extract in the course of the bio-assay is assessed also in terms of Na^+/K^+ variation. The fact that an observation (Na^+/K^+ ratio in urine of the patient) made by a non-biological method correlates so well with the results of the bio-assay seems strongly to point to a relationship between both variables.

Discussion

Previous Clinical Data

That the adrenal cortex might play an important rôle in the disturbances of electrolytes following surgical trauma had been suggested earlier by Pearson and Eliel (1949), Elkinton and Tarail (1950), and Mach (1954).

An important contribution has been made by Moore and Ball (1952), who made several attempts to reproduce under experimental conditions in man the metabolic changes which appear after operation. A mock operation with perfect reproduction of operative diet, management and ambulation, and with intentional lack of fear, pain, anæsthesia, tissue trauma, and adrenal discharge was carried out, with the result that among biochemical features the nitrogen metabolism resembled the postoperative pattern, but there was a lack of a sharp K^+ loss in the first day following operation.' On the other hand, a Na^+ loss was present instead of the well-known feature of Na^+ retention. When corticotrophin was given to reproduce the postoperative manifestations Moore and Ball observed the dose used here produced somewhat more 11-17-oxysteroid activity on the third and fourth postoperative day and less desoxy-like (salt conservation) on the first day. That corticotrophin does not increase aldosterone in the urine has also been shown by Cope and Llaurado (1954), Luetscher and Johnson (1954), and Venning et al. (1954).

A valuable and clear approach was made by Le Quesne (1953), who subdivided the manifest Na^+ retention after operation into two episodes called early sodium retention and late sodium retention, the former being specifically accompanied by acute K^+ excretion. Le Quesne pointed out that these two phenomena can be explained by a release of two different hormones from the adrenal cortex, each of which causes retention of Na^+. Moore (1953) has also indicated the possibility of a dissociation between activity like that of Compounds E and F and deoxycortone-like (salt-retaining) activity.

Previous Biochemical Data

Several investigators had previously shown that there is an increased excretion of cortico-adrenal steroids after operation, but hitherto no evidence of salt-conserving activity in the urine of postoperative patients had been reported. Weil and Browne (1939, 1940) reported as a result of their experiments using the cold-exposure test described by Selye and Schenker (1938) that urine of postoperative patients possesses material capable of protecting adrenalectomised rats against cold. Dorfman et al. (1942) found also by the cold-exposure test increased adrenocortical material in extracts of urine of postoperative male patients. Venning et al. (1943, 1944) found in human postoperative urine substances able to protect adrenalectomised rats against lethal action of low temperatures, to maintain life and growth of adrenalectomised rats, and to induce deposition of glycogen in the livers of fasted adrenalectomised rats. Cope and Hurlock (1954) found by paper chromatography for separating steroids that an operation such as gastrectomy causes a sharp rise of corticosteroids for several days. F

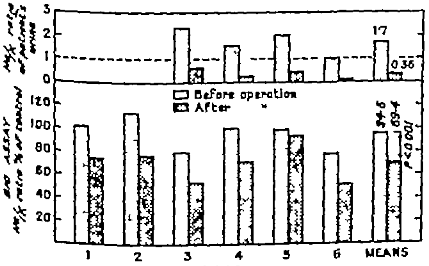


Fig. 2.—Upper scale, Na+/K+ ratio of patient's urine before and after operation; lower scale aldosterone activity of human urine before and after operation. Note correlation between scales.

1954), by estimating the level of 17 hydroxycorticoids in the blood, have also shown that there is a large increase of them after surgery

Although all these reports confirm the increased production and excretion of steroid materials after operation, it must be admitted that aldosterone by itself is not responsible for all these findings Despite the remarkable biological activity of the urine of patients after operation, the average excretion in terms of aldosterone in the twenty-four hours following operation is only 1 11 μg, a quantity so minute in comparison with the postoperative daily total steroid output of 6 3 mg (Cope and Hurlock 1954) that it is not surprising that variations in aldosterone excretion cannot yet be determined by chemical methods Thus Mach et al (1954) and Prunty et al (1954) have observed that there was no increase in the excretion of 17-ketosteroids or of 11-17-hydroxycorticoids when aldosterone in a dosage of 100–1050 μg daily was given to several patients It is for this reason that resort must be had to bio assay

To sum up, it can be concluded that, although several previous workers have shown increased activity of the adrenal cortex after surgical trauma, this activity was almost certainly due to 11-17-oxycorticoids, and hitherto there has been no evidence of changes of excretion of " salt conserving " hormone after operation The results of the present experiments prove conclusively that a " sodium retaining " factor is excreted immediately after operation simultaneously with a large loss of K^+ and an inversion of the urinary Na^+/K^+ ratio Since aldosterone has been chromatographically isolated (Cope and Llaurado 1954, Luetscher and Johnson 1954, Luetscher et al 1954) in the urine of patients having similar disturbances in electrolyte excretion, it appears highly probable that the factor in question is aldosterone Moreover increased excretion of this hormone after operation explains satisfactorily the sudden sharp inversion of electrolyte excretion forming part of the normal pattern of metabolic response to surgery

Although Moore (1953) cautiously stated that increased excretion of corticoids after operation does not necessarily mean overproduction of them, since this increased elimination might be due to alterations in the liver metabolism of, or in the kidney threshold for, steroids, this appears unlikely for the following reasons

(1) Prunty et al (1954) have recovered aldosterone from human urine after its administration

(2) The increased postoperative excretion of aldosterone accompanies the changes that theoretically would be expected from overproduction of this hormone, according to its biological activity—i e, sharp K^+ excretion and sudden Na^+ retention The administration of aldosterone reproduces the same pattern of electrolyte response (Na^+ retention and acute K^+ excretion) as after operation (Mach et al 1954, Kekwick and Pawan 1954)

(3) There is a remarkable chronological relationship between the onset of the aldosterone effect and the metabolic changes following surgery, as reported independently Mach et al (1954), on the one hand, showed that the influence of aldosterone on electrolyte excretion is evident three to six hours after injection, and, on the other hand, it is well known from the earlier work of Blixenkrône Møller (1940) that the sharp K^+ excretion following surgery begins within 6 hours after operation

(4) The amount of aldosterone excreted bears no relation to the 24 hour volume of urine If the cause of increased aldosterone excretion lay in the kidney, one would expect to find a relation between the total output of urine and the excretion of aldosterone, but there is none

(5) Franksson and Gemzell (1953) and Franksson et al (1954) have shown that there is a large increase of adrenocorticoids in the blood before the increased excretion in urine shown by other workers This may be taken as indirect evidence that a high output of aldosterone in the urine indicates a high concentration of this hormone in the blood

The detailed clinical observations of Moore and Ball (1952), Le Quesne (1953), and Moore (1953) have laid down the foundations for a thorough investigation b bio assay of the adrenocorticoids participating in th metabolic response to surgery Further research is sti needed to elucidate the factor or factors responsible fo " late sodium retention," to define the clinical impl cations, and to interpret the increased excretion aldosterone immediately following surgery Anoth promising field for investigation is the establishment the factors or substances stimulating or governing th production of aldosterone, since corticotrophin is not specific stimulus Selye (1950) suggested that the somat tropic hormone might be a specific stimulant of " mine alo corticoids," and Venning et al (1954) have reporte that, after administration of growth hormone, there an increase in the Na^+-retaining factor present in th urine of normal individuals If this finding is confirme by other workers, this relationship between aldosteron and growth hormone would be extremely interesting

In accordance with the new known facts about th regulation of electrolytes by the adrenal cortex it seen adequate to suggest that the terms " deoxycortone lik activity" and "mineralo corticoids" should be abandone and the more *logical* and *precise* " *aldosterone lik* activity " and " aldosterone-like corticoids " substitute

Apart from speculations it can be concluded that, wha ever steroids may be involved in the late sodium retentio the sharp loss of K^+ following surgery is associated wi *increased production of an electrolyte controlling adren* corticoid, which there is good reason to believe is ald sterone, and that overproduction of this steroid form part of the normal pattern of metabolic response surgery

Summary

By a bio assay designed to detect aldosterone it h been shown that a sodium retaining and potassiu excreting factor is present in the urine of patients aft surgical operations

Some patients excrete this factor before operation, b in all cases the excretion after operation is very muc greater than before operation

Evidence is adduced that this activity is due to ald sterone, the recently discovered electrolyte regulati cortico-adrenal hormone

The increased excretion of electrolyte regulati corticoid is shown to accompany the sharp potassiu loss and the early sodium retention which are comm features of the normal response to surgery Excreti levels of this corticoid correlate qualitatively with th Na^+/K^+ ratio in the urine of patients before and aft operation

Increased production of the electrolyte regulati corticoid may be one of the factors responsible for th electrolyte changes in the immediate postoperative perio

The results of assays with pure crystalline aldosteron are also reported This steroid is 100 times as strong deoxycortone when assayed in terms of Na^+/K^+ urinar deviation in the rat by the present method

I wish to thank Prof M F A. Woodruff and Dr C L Cop for their encouragement in this investigation and for criticis of the manuscript, Prof T Reichstein, of Basle, for a gi of pure crystalline aldosterone, and Mr G Spears fo assistance with the statistical analysis

REFERENCES

Blixenkrone Møller, N (1940) *Acta chir scand* 97 300
Chart J J, Shipley E S (1953) *J clin Invest* 32, 560
Conn J W (1954) *Brit med J* ii 1415
Cope C L, Hurlock, B (1954) *Clin Sci* 13 69
— Llaurado J G (1954) *Brit med J* i 1290
— — (1955) *J Endocrin* (in the press)
De Fourcroy A. F (1801) Système des connaissances chimique et de leurs applications aux phénomènes de la nature et de l'ar Paris (English translation by W Nicholson London 1804)
Desaulles P, Tripod, J Schuler, W (1953) *Schweiz med Woch* 83 1088
Dorfman, R I Horwitt, B N, Fish W R (1942) *Science*, 96 49
Elkinton, J R, Tarail R (1950) *Amer J Med* 9 200
Evans B M, Milne, M D (1954) *Brit med J* ii, 1067

References continued at foot of next column

A POSITIVE-NEGATIVE PRESSURE RESPIRATOR

G T SMITH CLARKE
M.I.Mech.E., F R.Ae.S
CHAIRMAN OF THE HOSPITAL MANAGEMENT COMMITTEE GROUP 20 BIRMINGHAM REGIONAL HOSPITAL BOARD

J F GALPINE
M D Leeds M.R C P.E., D.P.H D C H
MEDICAL SUPERINTENDENT WHITLEY HOSPITAL, COVENTRY WARWICKSHIRE

ARTIFICIAL respiration by intermittent positive pressure (I.P.P.) may contribute to the development of shock by lowering cardiac output (Astrup et al 1954) This is principally due to interference with venous return to the heart by raising the mean intrathoracic pressure Maloney and Whittenberger (1951a) say that I P P does not obstruct blood flow through the pulmonary capillary bed any more than does a normal inspiration producing the same degree of inflation In normal people receiving I.P.P the venous gradient is rapidly re established by a rise of systemic venous pressure but this may not happen if the vasomotor responses are compromised (Maloney et al. 1953)

To avoid this danger in I P P a method of giving adequate ventilation at an intrathoracic mean pressure approximating to atmospheric or even less is needed and this is possible by using negative pressure in expiration—i.e., positive negative pressure (P N P) Without the use of negative pressure the mean pressure in I P.P can be minimised by making inspiration as rapid as is consistent with satisfactory ventilation and by ensuring all possible freedom of expiration to allow a maximum of time for a pause after expiration at zero (i e atmospheric) level Apart from considerations of this sort Maloney et al (1953) state that the shape of the pressure curve is of little significance The use of negative pressure does not seem to have any direct effect on the rate of emptying of the lungs (Asmussen 1955) Fear of using negative airway pressure—especially of causing pulmonary œdema is considered groundless by Maloney and Handford (1954)

Certain pressure respirators are fitted with negative pressure devices on the Venturi principle Price et al (1954) studying some commercially available respirators speak of the high resistance in Venturi devices but found that a manually operated P N P apparatus with a negative pressure reservoir of large volume was capable of ventilating adequately at zero or negative mean mask pressure After testing a respirator having a Venturi attachment we concluded that the latter was largely ineffective probably because of swamping by the volume of positive pressure in the oncoming wave of expired air In these circumstances a Venturi becomes a potential obstacle owing to its narrow aperture In the new respirator the use of a pump ensures an adequate volume of negative pressure

An interesting comparison has been made by Maloney and Whittenberger (1951b) who consider that alternating negative and positive pressure applied to the body in a tank respirator are the physiological equivalents respectively of positive and negative pressure applied to the airways by a P N.P respirator

The usual type of pressure operated inspiratory-expiratory valve (P O valve) used with an I P P pump does not work satisfactorily with a negative pressure phase and the best solution of this is a mechanically operated inspiratory-expiratory valve (M. valve) as in the present machine This also abolishes any risk that the valve will stick as may happen with a P O valve A M valve offers negligible resistance to expiration if accurately timed and will never vary In contrast to this a P O valve must by definition have a resistance and is an inevitable (if small) obstacle to expiration It will moreover open later in the cycle if the build up of expiratory pressure is slowed by another resistance thus tending to magnify the effect of for example a small calibre endotracheal tube Thus a M valve offers definite advantages at any rate if for use over long periods and in conjunction with a P N P machine

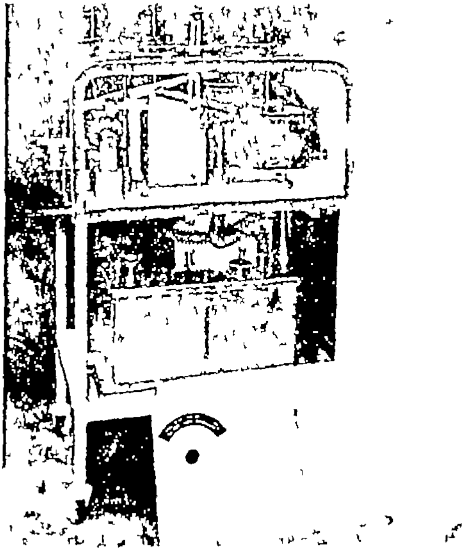


Fig 1—The respirator

DR. LLAURADO REFERENCES—*continued*

Frankson C Gemzell C A (1953) *Acta chir scand* 106 94
— — von Euler U S (1954) *J clin. Endocrin.* 14 609
Grundy H M., Simpson S A Tait J F (1952) *Nature Lond* 169 795
Keswick A. Pawan, G L S (1951) *Lancet* ii 162
Le Quesne L. P (1953) *Ann R. Coll Surg Engl* 13, 207
Llaurado, J G (1954) *Proc Univ Otago med Sch* 32 20
Luetscher J A jun Deming Q B Johnson B B (1952) *In* Wolstenholme, G E W Cameron M. P Ciba Foundation Colloquia on Endocrinology London, vol iv
— Johnson, B B (1954) *J clin. Invest* 33 276
— — Axelrad B J Oates J E. Sala G (1954) *J clin Endocrin* 14 812
Mach R. S (1954) *Schweiz med Wschr* 84 113
— Fabre J Duckert A Borth R. Ducommun P (1954) *Ibid*, p 407
Mills, I. H (1954) *Lancet* ii 814
Moore F D (1953) *Ann Surg* 137 289
— Ball, M. R (1952) The Metabolic Response to Surgery Springfield Ill
Pearson, O H, Eliel, L. P (1949) *J clin Invest* 28 803
Prunty F T G., McSwiney R. R. Mills, I H Smith M A (1954) *Lancet*, ii, 620
Schilling J A McCoord, A B Clausen S W Whelan, T J jun., Kuykendall S. J (1953) *Surg Gynec Obstet* 97 169
Selye H. (1950) The Physiology and Pathology of Exposure to Stress Montreal
— Schenker, V (1938) *Proc Soc exp Biol N Y* 39 518
Simpson, S A., Tait J F (1953) *Mem Soc Endocrin* no 2 9
— — Wettstein, A. Neher R. von Euw J Reichstein, T (1953) *Experientia* 9 333
— — — — — Schindler O Reichstein T (1954) *Ibid* 10 132, *Helv chim. Acta* 37 1163 1200
Swingle, W W, Maxwell, R., Ben, M. Baker, C. Le Brie S J., Eisler, M (1954) *Proc Soc exp Biol N Y* 86 11
Venning E. H Hoffman, M M. Browne J S L. (1943) *J biol. Chem.* 148 455
— — — (1944) *Endocrinology*, 35 49
— Carballeira A. Dyrenfurth, I (1954) *J clin Endocrin* 14 784
Weil, P., Browne J S. L. (1939) *Science* 90 445
— — (1940) *J clin Invest* 19 772
Wilkinson, A W Billing B H Nagy G Stewart C P (1950) *Lancet* ii, 735
Winfield J M., Fox, C L jun. Merzheimer W L. (1951) *Ann Surg* 134 626

The prototype respirator described below was wholly designed and constructed by one of us (G T S C)

Description of Machine

This respirator is designed to provide either P N P or I P P and to be reliable and efficient in both The construction is simple and robust, and any person of average ability can learn from the instruction plate (to be fitted to each machine) all that is necessary for efficient use and maintenance Apart from the driving motor and its switch no electronic apparatus is used There is no interference with radio or television when the machine is working It is essentially a hospital rather than a research apparatus

The machine is built as a complete unit (fig 1) It is mounted on castors and arranged in two tiers, the upper comprising the pumps, controls, driving motor, gearboxes, M valve, and mechanism for manual operation In an emergency the handle provided can be fitted on to the splined shaft at the front of the machine, it must be turned steadily at the required rate in the direction shown by the arrow The lower tier carries the humidifier, negative pressure vessel, and dry spirometer, and provides parking space for the handle for hand operation The apparatus is of suitable height to stand alongside a standard hospital bed

In addition to the motor switch, a "mains on" indicator, and a compound pressure gauge, there are four controls on the top of the cabinet

(1) The front transverse lever varies the stroke of the positive pressure pump and controls the volume of air (or air oxygen mixture) delivered It is calibrated in 15 stages from 200 c cm to 1500 c cm , representing air at atmospheric pressure pumped to the valve box at each stroke The minimal volume has been reduced to cater for the needs of children A dead weight safety valve is provided to blow off at a pressure of 30 cm water

(2) The lever on the left controls the "dog clutch" in the driving mechanism This has two positions the forward for emergency manual operation, and the rear for normal motor drive

(3) The central lever to the rear controls the stepless speed variations and gives breathing rates of 10–40 a minute This is calibrated in 10 steps of 3 and can be locked at any of these points This lever must not be moved when the machine is stopped It can be used unlocked if thought necessary to adjust rate to a finer degree as the patient recovers

(4) A circular knob on the right controls negative pressure, which is developed in a separate pump If it is set to minimum (as when using I P.P) negative pressure is zero, and expiration takes place through a disc valve (of negligible resistance) placed on the top of the negative pressure vessel When the control is turned towards maximum (– 20 cm water), the value can be read on the compound gauge, which measures pressures in the valve box

The Mechanical Inspiratory-expiratory Valve

We believe that this is the first mechanical respirator to be fitted with a M valve It is built into the side of the cabinet to reduce the length of tubing needed to reach the endotracheal-tube connection, this arrangement and the very small volume of the valve box keep "dead space" to a minimum The valve mechanism comprises two stainless steel poppet valves (inspiratory and expiratory) working in a housing of hard bronze They are closed by springs and operated by cams as in automobile and aero engines and timed so as not to be open together, however fractionally Modern valves of this type are reliable over long periods even when running at dull red heat and speeds of over 4000 revolutions a minute In the respirator working at room-temperature and at speeds about 15–20 a minute they should work indefinitely with minimal attention

The valve cams are designed to give a breathing pattern of inspiration 1, expiration 2 Since the inspiration period is 120° compared with a pressure stroke period of 180°, pressure is built up before the inspiratory valve opens This helps to overcome the inertia of the air in the humidifier and tubing and makes possible a "zero" period at the end of expiration when I P.P alone is in use If desired, the connections can be arranged to have the dry spirometer continuously in circuit, this is not detrimental to the breathing pattern if negative pressure is adjusted to compensate for the slight additional resistance to expiration

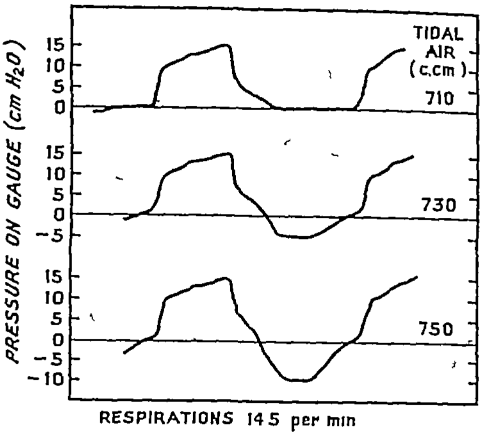


Fig 2—Pressure curves, close to tracheal tube, recorded by Dr Spalding during a clinical test of the respirator

The machine has been thoroughly tested with the aid of an "artificial lung" (Galpine and Smith Clarke 1955) which for this purpose was modified to record a negative as well as a positive pressure/volume curve We are indebted to Dr W Ritchie Russell and Dr J M K Spalding (Oxford), who tested the machine by using it to ventilate a tracheotomised adult female patient continuously for five days (fig 2) Apart from some minor suggestions they considered "the design and performance to be most promising"

REFERENCES

Asmussen E (1955) Proceedings of the Third Congress of the Scandinavian Society of Anæsthesiologists, p 22

Astrup, P Gotzche, H Neukirch, F (1954) *Brit med J* i 780

Galpine, J F Smith-Clarke, G T (1955) *Lancet*, i, 722

Maloney, J V jun , Elam, J O Handford S W , Balla, G A., Eastwood, D W , Brown, E S (1953) *J Amer med Ass.* **152**, 212

— Handford, S W (1954) *J appl Physiol* **6**, 453

— Whittenberger, J L (1951a) *Fed Proc* **10**, 88

— — (1951b) *Amer J med Sci* **221**, 425

Price, H L , Conner, E H , Dripps, R D (1951) *J appl Physiol* 6 517

FATAL HYPOGLYCÆMIA IN EARLY NON-ICTERIC INFECTIVE HEPATITIS

B E Tomlinson
M B Lond , M.R C P
PATHOLOGIST, GENERAL HOSPITAL, NEWCASTLE UPON TYNE

Hypoglycæmia due to liver disease was originally described by Nadler and Wolfer (1929) in a case of primary liver cell carcinoma Conn (1940, 1947) has reviewed spontaneous hypoglycæmia and described the liver disorders with which it may be associated

Hypoglycæmia in fulminant infective hepatitis is not uncommon Of 178 cases analysed by Lucké and Mallory (1946) a blood sugar level lower than 30 mg per 100 ml was recorded in 16 All these cases, however, showed massive destruction of liver cells, and the clinical diagnosis of severe liver disease was never in doubt

Death in the early stages of infective hepatitis is probably rare In the present case death took place in hypoglycæmic coma after a short illness and before the

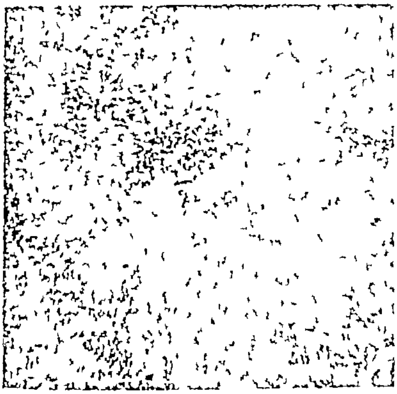


Fig. 1—Liver showing inflammatory infiltration of portal tract. (van Gieson. ×65.)

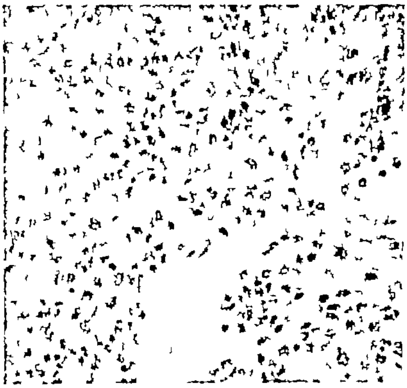


Fig. 2—Portal tract with cellular infiltration and vacuolated peripheral liver cells (Hæmatoxylin and eosin. ×270.)

onset of jaundice and although the liver histology resembled in most respects the findings in early mild infective hepatitis, the diagnosis could not have been made with certainty but for the subsequent development of jaundice in other members of the patient's family

Case-report

A girl, aged 6 years, was well and attending school until Nov 15 1953 when she developed a slight cough. On Nov 19 she had a sudden attack of vomiting and was sick about a dozen times. She vomited throughout the night but remained active and with no disturbance of consciousness. At 7 A.M on Nov 20 she fell asleep She called out several times during the first hour and vomited once but then fell into what her mother regarded as a deep sleep She was possibly unconscious from that time

On admission to hospital at 3 P.M on Nov 20 she was deeply unconscious, and ashy pale and could not be roused She had bitten her tongue Every 30 seconds or so she had a short spasm of generalised twitching Her respirations were slightly irregular and jerky No abnormal physical signs were elicited except that her muscle tone varied from minute to minute Her temperature was 97.4 F pulse rate 102 and blood pressure 108/60 mm Hg Investigations performed immediately showed Hb 13.2 g per 100 ml white cells 22 000 per c.mm serum sodium level 320 mg per 100 ml., serum-chloride level 375 mg per 100 ml, serum potassium level 31 mg per 100 ml alkali reserve 48.7 vol % blood urea level 64 mg per 100 ml and blood sugar level 15 mg per 100 ml Lumbar puncture produced clear cerebrospinal fluid under normal pressure with 6 lymphocytes per c.mm

Death took place within two hours of admission.

Necropsy findings eighteen hours after death were as follows. The *liver* weighed 610 g and was extremely pale Its cut surface showed yellowish grey liver lobules of normal size each accentuated by a narrow peripheral margin of reddish brown tissue The *spleen* was moderately enlarged (80 g) but otherwise showed no abnormality Numerous soft lymph nodes, measuring 0.5–1.5 cm across were present throughout the mesentery of the small intestine The largest node was over the head of the pancreas A few petechial hæmorrhages were present beneath the pleura and in the epicardium at the base of the heart

Histology.—There was a uniform infiltration of the portal tracts of the *liver* with lymphocytes a fair number of mononuclears of reticulo-endothelial type a few plasma cells, and eosinophils. This infiltration involved the periphery of the liver lobules, and in a few places was continuous with the infiltration of neighbouring portal tracts (fig 1) A few small foci of similar cells were scattered in other portions of the

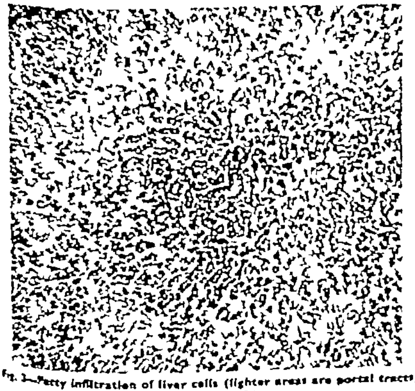


Fig. 3—Fatty infiltration of liver cells (lighter areas are portal tracts) (Sudan IV ×65.)

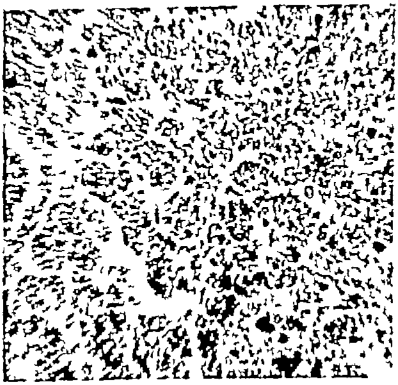


Fig 4—Intense fatty infiltration of liver cells. (Sudan ×270.)

liver lobules The peripheral sinusoids were congested, producing the red rims of the lobules already mentioned The liver cells showed diffuse and very fine vacuolation when stained with hæmatoxylin and eosin, only easily detected at the periphery of the lobules (fig 2) Staining for fat revealed an extreme degree of fine fatty infiltration of all the liver cells (figs 3 and 4), the severity of which was quite unexpected from the appearances of the hæmatoxylin and eosin sections In alcohol fixed material no glycogen was demonstrated *Although all the liver cells appeared equally affected by the* fatty infiltration, the related ischæmia of the centre of the lobules and slight irregularity of the liver cell cords suggested considerable swelling of the central cells and individual cells in other parts No evidence of centrilobular necrosis was found Reticulum stains showed no condensation around the central vein or elsewhere Occasional liver cells scattered throughout the lobules showed an intense eosinophilic degeneration accompanied by shrinking of the cells and rounding of the cell borders The nuclei of such cells were small and pyknotic A few liver cells in mitosis were seen and an occasional doubly nucleated cell There was diffuse lymphocitic hyperplasia in the mesenteric lymph nodes The large node over the pancreas was œdematous, with dilated sinusoids which had prominent lining cells and contained polymorphs and plasma cells The *spleen* was congested, with enlarged germinal centres, some showing cellular degeneration Many sinusoids contained considerable numbers of polymorphs The *kidneys* were congested, and there was a fairly well marked fine fatty infiltration of the proximal convoluted tubules, *with a few foci of necrosis in these tubules and the thick loops* of Henle

Subsequent Family History

Several days after this child's death her sister, aged 5 years, had a slight illness with vomiting, and a fortnight later she became jaundiced for several days, after which she rapidly recovered Five weeks later the dead child's twin brother became jaundiced but was only slightly ill. A few days later the mother became jaundiced, but again the illness was mild and of short duration The illness of the second twin was witnessed by the general practitioner who diagnosed infective hepatitis

Discussion

That the liver lesion was due to infective hepatitis is probable histologically and virtually certain in view of the subsequent family history

The liver changes in infective hepatitis have been extensively investigated since the publication of the aspiration biopsy studies of Roholm and Iversen (1939) Fatal cases show at necropsy almost complete destruction of liver cells (Lucké 1944, Lucké and Mallory 1946), and in many non fatal infections necrosis, particularly centrilobular, is well marked (Dible et al 1943) In the mildest instances, however, this rather characteristic centrilobular necrosis may be entirely absent, and the cellular degeneration limited to solitary cells showing distinctive eosinophilic change at any point in the lobule (Mallory 1947, Keller et al 1951) Lobular disarray, due to swelling and shrinking of liver cells, and evidence of regeneration of liver cells (mitotic figures and multinucleated cells) are often seen Bile thrombi are usually absent in the preicteric phase Even the mildest cases show severe portal infiltration, mostly with lymphocytes, reticulo endothelial cells, plasma cells, and eosinophils

The histological appearances of the liver in the present case are therefore, except for the fatty infiltration, identical with the changes found in mild infective hepatitis, as are also the lesions in the spleen, lymph-nodes, and kidneys

Fatty infiltration of the liver is unusual in infective hepatitis, particularly in the early stages (Weinbren 1952) Its severity and death in hypoglycæmia in the present case initially raised the question of poisoning, particularly by phosphorus or by mushrooms Detailed inquiries revealed no likely source of accidental consumption of any known liver toxin, and all the meals for several weeks had been taken by the rest of the family, *with the patient's twin eating identical food*

The possibility that the fatty liver and hypoglycæmia resulted from malnutrition, with or without an ingested toxic agent, and that the illness was similar to the fatty liver disease which occurs in the British West Indies (Waterlow 1948) did not bear examination The child was well nourished, as were the rest of the family, had no dietetic idiosyncrasies, and, apart from fairly frequent colds, was normal and healthy The illness did, however, resemble very strikingly the rapidly fatal form of "vomiting sickness" (Chambers 1953, Jelliffe and Stuart 1954), some cases of which terminate in hypoglycæmia

No explanation is available for the extensive fatty infiltration in the present case Death took place too rapidly for it to have been the result of the severe vomiting The appearances could result from infective hepatitis developing in a liver already the site of severe fatty infiltration To support this there would need to be evidence of some other factor likely to produce fatty infiltration No such evidence was found clinically or at necropsy That the fatty infiltration could be an unusual response of the liver to a mild attack of infective hepatitis cannot be denied but seems unlikely in the absence of even minor degrees of fatty change in the average case It seems rather more possible that the extensive fatty infiltration was a prenecrotic change in a severe hepatitis in which the development of extensive necrosis was forestalled by death in hypoglycæmia. This is pure speculation, for we have no knowledge of the early changes in the fulminant cases, and the development of necrosis and autolysis eliminates the possibility of demonstrating any pre-existing fatty infiltration

This child died before intravenous therapy could be started, and it is impossible to know whether the coma was reversible Jelliffe and Stuart (1954) record recovery from hypoglycæmic coma of short duration in vomiting sickness, but two patients who were in coma for more than seven hours died despite intensive therapy Treatment in such cases is obviously a matter of the greatest urgency, and only by keeping hypoglycæmia in mind as an occasional cause of sudden coma will any chance of recovery be possible

Summary

Fatal hypoglycæmia developed in the preicteric stage of infective hepatitis, being presumably related to severe fatty infiltration of the liver, a most unusual finding in this disease

Possibly this fatty infiltration represents a prenecrotic change in the liver cells in a case which otherwise presented the histological features of a mild hepatitis

I wish to thank Dr G Davison for permission to publish, Dr J Miller, the general practitioner, and Mr A Hall for the microphotographs

REFERENCES

Chambers, H D (1953) *W Ind med J* 2, 37
Conn J W (1940) *J Amer med Ass* 115 1669
— (1947) *Ibid* 134, 130
Dible J H McMichael J, Sherlock, S P V (1943) *Lancet* ii, 402
Jelliffe D B, Stuart K. L (1954) *Brit med J* i 75
Keller T C, Gigcs B Smetana, H F (1951) *Milit Surg* 109, 425
Lucké, B (1944) *Amer J Path* 20 471
— Mallory, T (1946) *Ibid*, 22, 867
Mallory T B (1947) *J Amer med Ass* 134, 655
Nadler W H, Wolfer, J A (1929) *Arch. intern Med* 44, 700
Roholm, K Iversen P (1939) *Acta path microbiol scand* 16, 427
Waterlow J C (1948) *Spec Rep Ser med Res Coun Lond.* no 263
Weinbren K (1952) *J Path Bact* 64 395

NUTRITION AND FLUID AND ELECTROLYTE BALANCE DURING TREATMENT OF TETANUS

G WILSON
M B Leeds, F R C S
REGISTRAR IN GENITO-URINARY SURGERY THE GENERAL INFIRMARY AND ST JAMES'S HOSPITAL LEEDS

A. D CARE
M A Camb Ph.D Leeds
RESEARCH FELLOW IN UROLOGY IN THE UNIVERSITY OF LEEDS

A BOY aged 15 was admitted with a severe degree of tetanus and kept unconscious for fourteen days with nitrous oxide administered through a tracheotomy tube Convulsions were controlled with a continuous intravenous infusion of suxamethonium chloride (J L Ablett 1954 personal communication)

It was thought that the anæsthesia might have to be continued for three weeks, and that therefore artificial feeding and a fairly strict check on fluid and electrolyte balance would be necessary Few details of nutrition and of the administration of fluids in such cases have been published (Forrester 1954 Honey et al 1954, Lassen et al 1954, Shackleton 1954) The need for adequate nourishment is obvious but careful control of the fluid and electrolyte balance is of paramount importance because the control of convulsions with a continuous infusion of suxamethonium chloride may necessitate the intravenous administration of several litres of fluid daily

Nutrition

No details of the patient's height and weight had been recorded, but it was estimated that his basal metabolic requirements would be about 1500 calories per 24 hr because he was to be kept at complete rest by the administration of relaxants About 900 ml of the following concentrated gruel was given, by stomach tube in four divided doses a day, the tube being removed after each feed

1½ pints of fresh milk 2 eggs 4 oz glucose 1 oz Casilan 2 oz dried milk 1 teaspoonful Marmite 1 tablet (100 mg) ascorbic acid ½ teaspoonful salt	Carbohydrate 208 g Protein 87 g Fat 60 g

The total calorific value was about 1500 calories and the electrolyte content was as follows

Sodium	123·0 m.eq per litre
Potassium	52·4
Chloride	134·0
Calcium	100·0 „

The concentrated feed together with the intravenous fluids administered (see below), gave the patient a daily intake of 1800–2100 calories

No regurgitation developed but with this complication in mind, the provision of more frequent and smaller feeds and the intravenous administration of 20% glucose were considered as alternatives to the routine adopted

Fluid and Electrolytes

Since the water content of the concentrated stomach feed was less than 1 litre intravenous fluids were given to supplement this In calculating the amount of fluid required the following factors were taken into account: (1) insensible losses via skin and lungs (about 1000 ml per 24 hr) (2) output of urine (1000 ml) and (3) excessive losses due to anæsthesia artificial respiration, and sweating which was at times profuse

It was decided that the fluid to be administered should contain sufficient electrolytes to cover normal losses and should be so composed that if the anæsthetist wished an extra 1–2 litres of fluid could be given without danger of overhydration

The solution chosen for intravenous infusion was Howarth's (1954) solution C

Glucose	33 g	approx. 135 calories	
NaCl	3 g	51·3 m eq of Na	+ 70·3 m eq of Cl
KCl	1 g	13·4 „ K	
CaCl	0·2 g	3·6 „ Ca	
MgCl	0·1 g	2·1 „ Mg	
Aqua ad	1000 ml		

From 2 to 4 litres was administered per 24 hours. Together with the stomach feeds this gave a total fluid intake of 3–5 litres a day On this régime the daily output of urine was 1500–3800 ml

The intravenous fluid was administered through an indwelling polyethylene tube so that the patient could be turned frequently without difficulty No major complication developed from the use of such a tube but minor accidents necessitated a change in the site of the drip on three occasions

Collection of Urine Specimens

The patient developed an automatic bladder which emptied whenever he was turned in bed Catheterisation was therefore unnecessary, and little difficulty was experienced in collecting the urine specimens

Discussion

Nutrition

When the patient was weighed about three weeks after admission he scaled 94 lb and ten days later he had increased to 102 lb He had therefore probably lost during his illness well over 14 lb despite what was considered to be a reasonable intake of nourishment which included 87 g of protein

A possible explanation for this loss of weight might be that the patient was in negative nitrogen balance If this were so alternative mechanisms may be postulated:

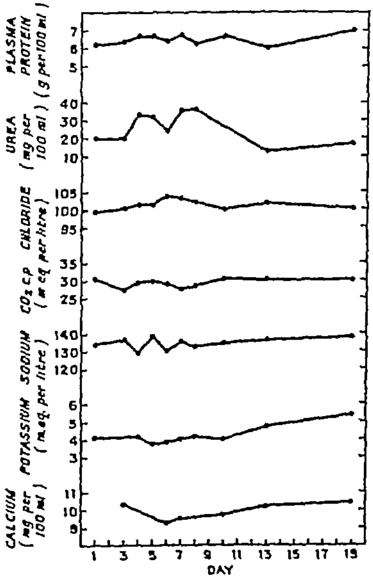


Fig 1—Blood analyses.

CORRELATION BETWEEN INTAKE AND URINARY EXCRETION OF SODIUM, CHLORIDE, POTASSIUM, AND CALCIUM IONS

Day no	Fluids (ml)			Na (m eq)			Cl (m.eq)			K (m eq)			Ca (m.eq)		
	Total intake	Urinary output	Diff.	Total intake	Urinary output	Diff	Total intake	Urinary output	Diff	Total intake	Urinary output	Diff.	Total intake	Urinary output	Diff
1	2690	3850	−1160	186	234	−48	230	345	−115	63	109	−46	76	25	51
2	3660	—	—	232	—	—	295	—	—	75	—	—	77	—	—
3	4300	2580	1720	282	91	191	356	205	151	93	78	15	102	—	—
4	5200	2690	2510	350	103	247	437	200	237	117	86	31	134	14	20
5	4400	2200	2200	387	147	240	363	231	132	94	77	17	103	28	75
6	2900	2990	−90	212	224	−12	259	290	−31	74	74	0	97	26	71
7	3900	1660	2240	262	118	144	328	191	137	87	67	20	101	—	—
8	3300	2250	1050	210	172	38	267	241	26	67	77	−10	70	22	48
9	4200	2370	1830	300	192	108	368	258	110	103	80	23	131	24	107
10	3900	2270	1630	262	137	125	328	239	89	87	90	−3	101	24	77
11	3900	3680	220	262	346	−84	328	380	−52	87	72	15	101	34	67
12	5900	2698	3202	325	216	109	425	259	166	98	80	18	78	23	55

(1) The administration of the anæsthetic, or the disease process per se, may have led to excessive breakdown of protein, possibly brought about by an increase in adreno cortical activity

(2) Prolonged muscular paralysis produced by the administration of relaxants may cause rapid loss of muscle comparable to that which follows denervation

Where there is a substantial breakdown of tissue, however, it is customary to find a concomitant negative potassium balance (Gamble et al 1923), of which there was no evidence in this patient (see below) Nevertheless it is felt that full balance studies would be well worth while in similar cases

Blood Analyses

Throughout twenty days, during which blood analyses were frequently performed, no gross deviation from the normal took place (fig 1) despite the fact that there was profuse sweating from time to time and that, during the transitional period from artificial to natural feeding, the patient had watery diarrhœa lasting three days

Urine Analyses

The results of the daily urine analysis are set out in fig 2 Approximate fluid and electrolyte balances were obtained by correlating total intake and urinary excretion (see table)

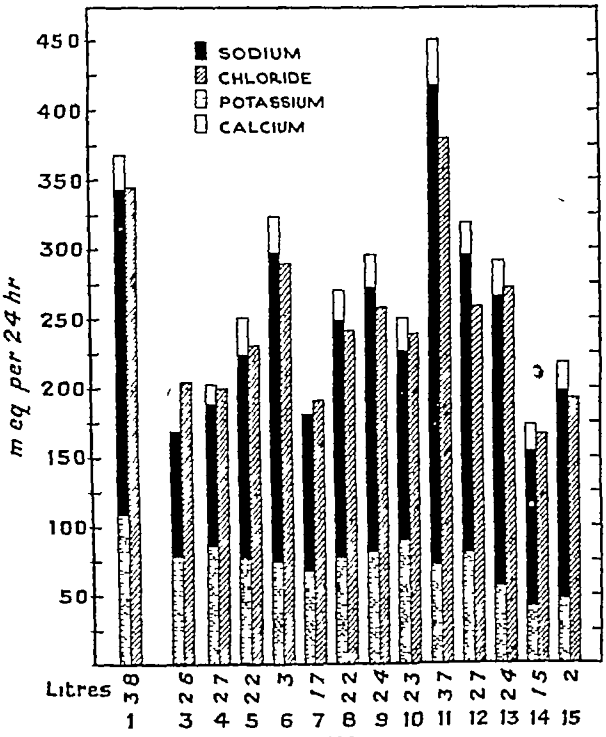


Fig 2—Urine analyses

Since the apparent gains of sodium and chloride ions by the body were in amounts equivalent to one another and, moreover, closely followed the gain of fluid, it was concluded that sweating might have been sufficient to account for this discrepancy An approximate calculation reveals a total apparent gain by the body of sodium chloride of 87 m eq a day This figure could be accounted for not only by the experimental errors involved in collecting the urine but also by the salt lost in the profuse sweating (average composition of sweat 25 m eq of sodium chloride per litre), in the aspiration of bronchial secretion, and in the saliva and fæces (saliva contains 10 m eq of sodium chloride per litre, and fæces contain about 2% of the total intake of sodium [Peters and van Slyke 1932] but no chloride)

In addition to the total salt content of the body, attention must also be paid to any alterations in its total potassium content In the present case the apparent total gain of potassium in the period studied was 80 m eq The potassium content of the fæces in the same period could be taken as 8% of the total intake of potassium (Peters and van Slyke 1932)—i e , 75 m eq Since the plasma potassium level remained normal, the residual 7 m eq of potassium was presumably lost in the saliva and bronchial secretions (saliva contains about 25 m eq of potassium per litre)

The urinary output of calcium was often as much as 26 m eq per 24 hours, but this probably reflects the large intake of calcium and the fact that the patient was totally recumbent The amount of calcium in the fæces was not estimated , hence the exact state of calcium balance was unknown

Summary

The nutrition and fluid and electrolyte balance in a case of tetanus are reported

Blood analyses over twenty days showed no significant deviation from normal

A satisfactory correlation was obtained between the administration and the excretion of fluid and electrolytes

We wish to thank Dr H G Garland for allowing us to investigate his patient , the staff of the department of urology for their technical and secretarial assistance , and Mr J Hainsworth and Miss C E Campbell, of the department of medical photography, St James's Hospital, for the illustrations

REFERENCES

Forrester A T T (1954) *Brit med J* ii 342
Gamble J L Ross, G S Tisdall F F (1923) *J biol Chem* 57 633
Honey G E Dwyer B E Smith, A C. Spalding J M K (1954) *Brit med J* ii, 442
Howarth A T (1954) *Univ Leeds med J* 3 87
Lassen H C A Bjorneboe M Ibsen B Neukirch, F (1954) *Lancet* ii 1040
Peters J P van Slyke D D (1932) Quantitative Clinical Chemistry London , vol i
Shackleton, P (1954) *Lancet* ii, 155

LEIOMYOSARCOMA OF THE STOMACH
WITH INTRAPERITONEAL PERFORATION

J F HORLEY
M.B Lond.
PATHOLOGIST ROYAL SUSSEX COUNTY HOSPITAL, BRIGHTON, SUSSEX

REPORTS of leiomyosarcoma of the stomach are sufficiently uncommon for individual examples to deserve attention on this account alone Moreover because the prognosis with suitable treatment may be excellent the importance of distinguishing this neoplasm from carcinoma of the stomach makes its recognition especially important

The incidence is difficult to compute accurately for many reports have been concerned with single examples Watson (1950) states that most authorities accept an incidence of 1 case in every 1000 malignant gastric neoplasms. However Marvin and Walters (1948) found in the records of the Mayo Clinic for 1907–47 16 cases among 10 000 surgically verified cases of gastric carcinoma, an incidence of 1 in 625 but 10 of these had occurred in 1940–47 Marshall and Meissner (1950) found 9 cases of leiomyosarcoma in 1171 operations for malignant growths of the stomach and Cowdell (1950) described 5 examples found among 370 gastric neoplasms These figures suggest that the present incidence may be about 1 in every 100 gastric malignant growths

Whatever the true incidence may be its importance can never be judged by weight of numbers alone for if it is recognised there may be a chance of cure in a patient who would be considered hopelessly inoperable had he a gastric carcinoma of similar extent

Case report

A man, aged 40, was admitted to the Royal Sussex County Hospital complaining of severe pain on the left side of the abdomen of sudden onset for the past 6 months he had had discomfort in his epigastrium

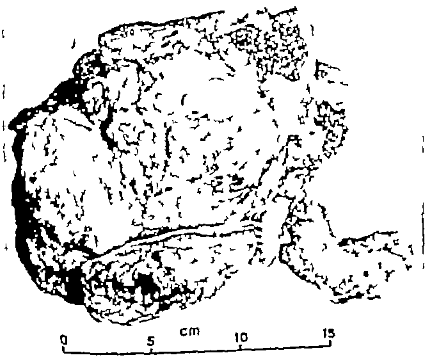
On examination he was restless sweating and in pain with blood pressure 105/70 mm Hg His abdomen was distended and tender with guarding and some rigidity of the left side Bowel sounds were diminished Clinically a perforated viscus was suspected

Laparotomy was done by Mr W R. Forrester Wood A large cystic swelling was found adherent to the stomach and transverse colon and had perforated into the lesser sac It was considered impossible to remove the tumour at that time instead it was incised and drained of some 30 oz of dark fluid The abdomen was closed with drainage of the neoplasm and lesser sac

Postoperatively the hæmoglobin was 92% (100% = 14 8 g) Subsequently in spite of intravenous therapy the blood urea level rose to 178 mg per 100 ml. on the tenth postoperative day and twenty four hours later the patient died

Necropsy twenty four hours later showed no evidence of recent loss of weight In the abdomen was found a tumour with irregular contours but roughly spherical (see figure) and measuring 21 × 16 × 10 cm Its centre had degenerated and been discharged leaving a wall which varied in thickness from 3 cm. to paper thinness and was firm and rubbery in consistence Two perforations of this cystic neoplasm led into the peritoneal cavity one opened into the lesser sac and the other was the aperture through which the tumour had been drained to the surface at operation. The neoplasm was adherent to the transverse colon and the spleen, but the adhesions could be broken down easily It was blended intimately with the tail and body of the pancreas and one segment of the growth formed part of the wall of the stomach A perforation of the gastric mucosa, measuring 2 × 1 cm. opened into the centre of the neoplasm and thus communicated with the two perforations already mentioned All the remaining organs of the body were normal in particular no metastasis was found.

Microscopy—Sections taken from many parts of the neoplasm were stained with hæmatoxylin and eosin Van Gieson, phosphotungstic acid hæmatoxylin and Mallory's trichrome stains The tumour consisted chiefly of fusiform cells which stained like smooth muscle The morphology and arrangement of the cells varied considerably in different parts of the neoplasm in some there was a very regular pattern of interlacing fibres with few mitotic figures in others the cells were plumper and pleomorphic with 2–3 mitotic figures per high power field The tumour had broken through the muscularis mucosa of the gastric wall and was nowhere completely encapsulated It was growing well into the substance of the pancreas but except in a few places the growing edge was tipped with a layer of fibroblasts and round cells The appearances were those of a leiomyosarcoma of the stomach



Leiomyosarcoma of stomach: complete specimen. Tail of pancreas can be seen emerging from right border Uppermost perforation led into lesser sac.

Discussion

Leiomyosarcoma of the stomach is described as endogastric when the main bulk of the tumour usually sessile lies within the lumen of the stomach and exogastric when it expands outside it According to Golden and Stout (1941) these tumours occur with equal frequency in either sex and may be found at any age

To the naked eye the tumours are usually irregularly lobulated and to the touch they are firm and rubbery quite unlike stony hard and friable carcinoma Pedunculation with cyst formation from central degeneration of the neoplasm is not uncommon in the exogastric type Extension of growth takes place by slow expansion and the tumour's invasive powers are usually slight hence metastases are slow to develop and were seen in less than 20% of the reported examples However a few cases such as that of Lyons and Schneider (1943) have been described in which widespread metastases were found in the presence of a relatively small primary growth

Microscopically, increased mitotic activity and invasion of neighbouring organs may be found but parts of the tumour especially in isolation may be difficult to distinguish from simple leiomyomas. For this reason and because the term leiomyosarcoma although histologically correct may suggest erroneously a highly malignant neoplasm Golden and Stout (1941) prefer to describe them as malignant leiomyomas.

Clinically, leiomyosarcoma of the stomach especially the exogastric type may be completely silent until some complication arises Intestinal blood loss from ulceration of the overlying gastric mucosa may lead to severe and progressive anæmia and this combined with the paradoxical coupling of a large epigastric tumour with slight loss of weight may enable the diagnosis to be made preoperatively

The present case is unusual in several ways Anæmia was not a feature and the tumour although large was not palpable possibly because of cystic degeneration

Perforation into the peritoneal cavity, causing an acute abdominal emergency, has been reported previously only 5 times in 4 (Fritzsche 1918, Baumgartner 1939, Mass and Kirshbaum 1940, Golden and Stout 1941) it was fatal, but in 1 (Shepherd 1950) resection was followed by recovery In 3 of these 5 cases the tumour was mistaken before necropsy for a perforated gastric carcinoma

Summary

A case of leiomyosarcoma of the stomach with perforation into the peritoneal cavity is described

Leiomyosarcoma of the stomach is diagnosed more often nowadays and may not be so uncommon as used to be supposed

Such cases repay diagnosis because the prognosis is good after surgical excision

I wish to thank Mr Forrester Wood for allowing me to report a case admitted under his care and for the interest he has shown in the preparation of this paper

REFERENCES

Baumgartner C J (1939) *West J Surg* **47** 27
Cowdell, R H (1950) *Brit J Surg* **38**, 3
Fritzsche R (1918) *KorrespBl schweiz Arz* **48**, 1273
Golden T Stout A P (1941) *Surg Gynec Obstet* **73**, 784
Lyons C G, Schneider M (1943) *Amer J Roentgenol.* **49**, 393
Marshall S F, Meissner W A (1950) *Ann Surg* **131**, 824
Marvin C P Walters, W (1948) *Arch Surg* **57**, 62
Mass, M Kirshbaum J D (1940) *Amer J Roentgenol* **44** 710
Shepherd J A (1950) *Brit J Surg* **37** 479
Watson K (1950) *Ibid*, p 21

LEIOMYOMA OF THE STOMACH

AN UNUSUAL CASE

H R Ker
M B Lond, F.R C S
SURGICAL REGISTRAR, CHARING CROSS HOSPITAL GROUP,
WEMBLEY HOSPITAL

Myoma of the stomach is not an exceptionally rare tumour Aird (1949) states that it occurs once in every 2000 gastric neoplasms It may be pedunculated and attached to the serous or mucous aspects of the stomach, and usually presents by causing pyloric obstruction or ulceration of a submucous growth The case here described is of interest because the only symptom was nocturnal dyspepsia, present for some years, and because of the unusual manner in which it finally became an emergency

Case-report

The patient was a fit retired Guards' officer of 77 On Feb 18, 1955, he slipped and fell on ice, and was brought to Wembley Hospital complaining of pain in the left hip Clinical and radiological examination showed an intracapsular fracture of the neck of the left femur, and he was admitted for pinning

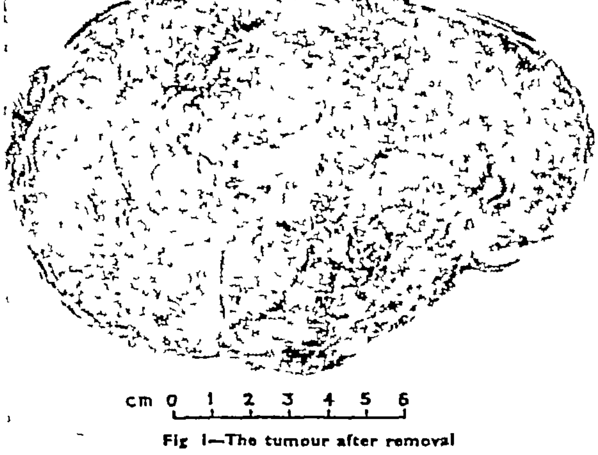


Fig 1—The tumour after removal

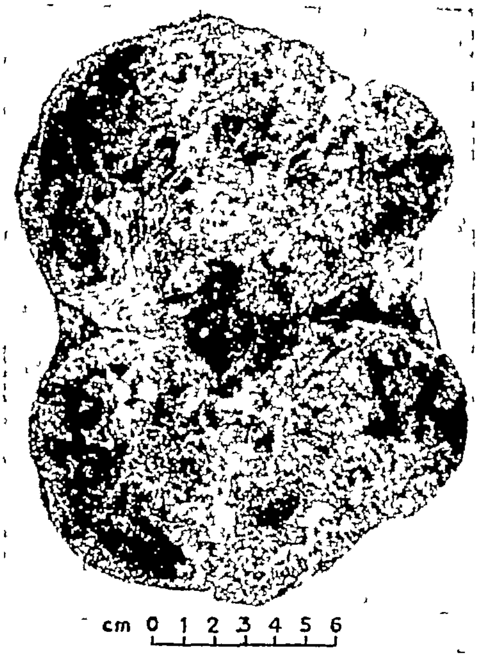


Fig 2—The cut surface of the tumour

In the course of routine preoperative examination he stated that he was perfectly well except for nocturnal dyspepsia, from which he had suffered for about seven years There was a slight feeling of fullness after meals during the day, but when he retired to bed he would get colicky epigastric pain, and would vomit a small amount of bile stained fluid almost every night The house surgeon discovered a round, mobile, non tender tumour, the size of a grapefruit, situated in the epigastrium just to the right of the midline The only other abnormality was a hydrocele of the right tunica vaginalis

It was felt that the treatment of his fracture was of more urgent importance than his abdominal tumour, and as X-ray examination did not reveal any evidence of a secondary deposit, a Smith Petersen pin was inserted by Mr A J Cokkinis on Feb 24

Postoperative progress was satisfactory, apart from his old feeling of epigastric discomfort, and bilious regurgitation on the first day On Feb 26 he complained of more pain, and the vomiting became more severe A milk drip was tried, but this did not relieve him, and an intravenous drip with gastric aspiration was set up

I first saw him on the 4th postoperative day, by which time he had been on intravenous fluids for three days He had been taking fluids by mouth, but the aspirations had exceeded the intake by about 3 oz per day He was a thin man, with a hard round mobile tumour in the epigastrium to the left of the midline This fact was pointed out to the houseman, who announced himself to be undismayed—the tumour had been on the right on admission, and if it chose to move, he could not hold himself responsible for it At this stage it was found that a barium meal performed at the request of his own doctor in 1949 was available This showed that the stomach and first part of the duodenum were pushed to the left apparently by some radiotranslucent body These films had been taken with the patient standing There had apparently been no clinical evidence of a tumour at that time

It was decided that since gastric obstruction was complete, laparotomy must be performed The provisional diagnosis was carcinoma of the stomach, or pancreatic cyst

Operation

On March 1, after anæsthesia had been induced by Dr R J Clausen, the abdomen was palpated, and the tumour could not be felt at all in the epigastrium The abdomen was opened through a left paramedian incision A large tumour 15 cm. by 12 cm (figs 1 and 2) was found in front of the descending colon just below the level of the umbilicus When it was delivered into the wound, it was found to be attached to the centre of the lesser curvature of the stomach by a pedicle three fingers breadth across, in which were running large blood vessels. The tumour by moving to the left had caused a partial volvulus of the stomach. There were no secondary deposits, and no other cause of intestinal obstruction could be found.

The pedicle was ligatured in three bites, the tumour removed, the raw area buried in peritoneum, and the abdomen closed.

Postoperatively, the patient's condition improved rapidly. The Ryle tube was removed on the following day and he resumed a full diet on the fourth postoperative day. [illegible] the rest of the stay in hospital necessitated by his fractured femur, he suffered no dyspepsia, either lying or standing. When seen in outpatients two months later he stated that his old pain and vomiting had completely gone. The microscopic section of the tumour showed a typical myoma with no evidence of malignancy.

Discussion

It seems, from the history, the size of the tumour and the previous barium meal, that this tumour had been present for at least seven years. It apparently caused little trouble when the patient was standing upright, but when he lay down at night, it slipped to the left, falling into the hollow at the side of the lumbar vertebral bodies, causing a partial volvulus of the stomach and his pain and vomiting. This was well seen when the patient was relaxed under anæsthesia and the tumour then descended even further on the left and could not be felt in the epigastrium. When he took to his bed after the pinning of his femur, the tumour was unable to return to its normal position and obstruction became complete.

I wish to thank Mr A J Cokkinis for his permission to report this case.

REFERENCE

Aird, I (1949) Companion in Surgical Studies. London.

Medical Societies

BRITISH ORTHOPÆDIC ASSOCIATION AND SOCIETE FRANCAISE D'ORTHOPEDIE ET DE TRAUMATOLOGIE

On May 5–7 the association and the society held a combined meeting in Paris under the chairmanship of their presidents, Prof Bryan McFarland and Prof P Padovani.

Surgery of the Paralysed Lower Limb

Equalisation of Length

Mr R I Stirling (Edinburgh) said that when shortening of the longer limb was indicated he preferred, in the case of the femur, a long oblique osteotomy of the mid-shaft fixed by transverse screws after the necessary overlap. Union was certain, which it was not after transverse resections, and he disliked the subtrochanteric operations because of possible damage to the blood supply of the epiphyseal region and later osteo-arthritis. Stapling of the epiphyses was uncertain and in any case would not provide more than an inch of shortening. In the tibia he used a Z resection. $1^1/_2$ inches of shortening was the limit acceptable at one operation, but it could be repeated later. The calf muscles were sometimes slow to recover, and a raised heel for a while was helpful.

In bone-lengthening operations the counter pressure points should be in the bone itself and not beyond a joint for fear of overstretching the ligaments. Equally one must beware of damaging a joint surface by undue pressure. He used four pins in the same bone, and in the case of the femur took care to distract the knee first. He used a Z-osteotomy in both femur and tibia and emphasised the importance of complete division of periosteum and fascia. In the case of the tibia there was grave danger that the lower end of the fibula might lag behind, rendering the ankle joint unstable, and he therefore preferred now to fuse the lower end of the fibula diaphysis to that of the tibia, particularly if the lower end of the fibula already lay unduly high.

A poor circulation already present in the limb was no contraindication to bone lengthening. The best age was 11–13, but it could be done earlier if the difference in length was not altering [illegible] in a completely flail limb. Over the age of 16 union was much slower to occur. In cases of partial paralysis bone-lengthening operations often altered the muscle balance, so that they should precede any stabilisation or tendon transplant operations. If the muscles were already balanced it was usually better to shorten the other limb.

In 120 cases he had had only 4 of interference with the peripheral circulation and all recovered; the increase should not exceed $^1/_{16}$ inch per day. The incidence of subsequent arthritis had not been significant, and any distortion of the foot was usually easily corrected by manipulation.

Paralytic Lesion of the Hip with Particular Reference to Dislocation

G Blundell Jones (Exeter) remarked that the inherent stability of the hip could be spoilt by the presence of contractures or by alterations of the bony contours. Paralysis led to coxa valga, and coxa valga was a potent cause of dislocation. Pelvic obliquity might be due to contractures of either hip or trunk. With regard to corrective procedures he thought that it was probably impossible by tendon transplant to replace the hip abductors. Mustard's iliopsoas transplant was the most effective method. Osteotomy of the base of the femoral neck fixed with a Capener plate was very satisfactory for marked coxa valga, and not only in paralytic cases. In spastic cases preliminary tenotomies and occasionally shortening of the femoral shaft might be required. He remarked that the onset of paralysis after the age of 2 might lead to coxa valga but rarely to dislocation; dislocation was almost always the result of poliomyelitis in infancy. Shelf operations or arthrodesis were rarely indicated. In planning treatment the degree of coxa valga, rotational deformity, and condition of the acetabulum all needed assessing. If arthrodesis was required he thought the Charnley central dislocation procedure was the best.

Tendon Transposition in the Buttock and Thigh

Mr J M P Clark (Leeds) thought that the revulsion which followed the first enthusiasm with which the work of Robert Jones and Tubby was greeted was now on the wane. It was important to realise that it was impossible to replace a completely paralysed muscle, that no muscle training will ever alter muscle imbalance, and that deformities may recur even after arthrodesis. Tendon transposition was best done to prevent deformity, and transplants needed protection for at least six months after operation.

Replacement of hip abductors was most difficult; the iliopsoas transplant was satisfactory if a normal gluteus maximus and sartorius were present, but it was a severe operation. In the presence of a good gluteus maximus the backward shifting of the origin of tensor fasciæ femoris could help a weak gluteus medius.

In adduction deformity tenotomy, [illegible] and osteotomy all had a place. In preventing [illegible] of the deformity he had successfully tried a [illegible] in which the adductor origin detached from the [illegible] and mobilised with nerve-supply intact was transposed [illegible] femoris and attached to the iliotibial band.

In the case of the knee transference of the quadriceps could be done (1) to prevent [illegible] in a calliper to be discarded, or (3) to prevent [illegible] deformity of the knee. They were most [illegible] the foot was stable and any knee deformity had [illegible] and in the presence of strong hamstrings [illegible] fair plates. [illegible] tendinosus and gracilis [illegible] biceps laterally [illegible] all used, but semimembranosus [illegible] intact. [illegible] stressed the importance of [illegible] coupled action [illegible] hamstrings with the [illegible] the last part [illegible] length movement of [illegible] knee, which [illegible] the big transplant a good [illegible] sartorius and [illegible] effect of this femoris had not been [illegible] reservoir [illegible]

Tendon Transp[illegible] Foot

Mr D M [illegible] said that the [illegible] easy, could [illegible] and did no [illegible] but unfortunately [illegible] a third [illegible] Equinus deformity [illegible] calcaneus [illegible] was [illegible] and [illegible] the [illegible] the big toe region, and instruments were useless in their control.

One must know accurately the power of muscles and what the deforming muscles were—a matter difficult to assess before the age of 5. It was useless to employ as a transplant a muscle whose automatic phase of function was at variance with that of the recipient; hence the futility of transplanting tibialis anterior to the calf. The essential principles were that full passive correction should be possible, the deforming force must be removed, and the paralysed muscle action must be replaced.

Transplants of the peronei to the calf in cases of calcaneo-cavus with or without valgus had failed in more than half of 40 cases. Transplanting extensor hallucis longus to the first metatarsal neck failed in 24 of 39 cases of pronation of the forefoot, and in a similar proportion transposing peronei to the dorsum of the foot failed to improve plano-valgus. The most successful group was that of equinovarus deformities, where only 9 out of 22 failed to give improvement; 6 of the failures were due to the later disinsertion of the transplant from its new attachment. In all groups secondary deformity was not uncommon.

Mr Brooks concluded that despite the many failures tendon transposition was a useful mitigating procedure in carefully selected cases as long as the cause of the original deformity had been eradicated; he doubted whether it was ever worth shifting a muscle which was not itself causing the deformity.

Operations for Relieving Paralysis of Intrinsic Muscles of Toes

Mr T. T. Stamm (London) said that the Lambrinudi procedure of multiple interphalangeal fusions transferred the activity of the flexors from the interphalangeal to the metatarso-phalangeal joints. When the operation was originally designed it was proposed to attack the accompanying cavus deformity six months later, but this had proved unnecessary since successful toe fusions were found to cure the cavus also. For this operation to succeed there must be no fixed deformity of the metatarso-phalangeal joints. Bony fusion must be produced; fibrous ankylosis gave rise to pain. The insertion of axial Kirschner wires produced too many failures of bony fusion; he thought that the best method was to tie the toes down to a Lambrinudi footplate and to leave the splint on for six weeks. The optimum position was slight flexion of the proximal and slight hyperextension of the distal interphalangeal joint.

If there was fixed extension of the metatarso-phalangeal joints, multiple tendon transplants of the long flexors of the toes to the extensors was a better operation, but this was contra-indicated if there was much fixed flexion of the proximal interphalangeal joints. The two procedures were complimentary and should not be looked on simply as alternatives for any given case. Failures were due to choice of the wrong operation, faults in technique, and occasionally absence of bony fusion.

He considered that the operation of transplanting the extensor tendons into the metatarsal necks was a poor one; it was unsound physiologically because the timing of the automatic action of these muscles was wrong for the new function required of them, and in any case the tendons seemed to return by magic to their original insertions.

In the subsequent discussion Mr H. J. Seddon (London) spoke of the need for independent assessment of a surgeon's results from tendon transplants in the foot; the basic idea was good, but fewer cases than were supposed were in reality worth operating on. Prof K. E. Kallio (Helsinki) showed a film of his operation for arthroplasty of the hip, using a cap of skin taken from the abdomen to cover the femoral head.

Osteochondritis of the Hip

Experimental Study

Dr J. Lemoine, working with Dr R. Lagrange, largely at Oxford, had operated on sixty rabbits 2–3 weeks old. Ligation of the anterior circumflex vessels was found to produce only minimal changes, but ligation of the round ligament was followed by varying degrees of enlargement of the femoral head, with flattening, increased radiographic density, and often some subluxation. Angiograms showed increased vascularity of the head. The neck of the femur often thickened and both macroscopically and microscopically the changes were very similar to those seen in Perthes disease.

Perthes Disease

Prof M. Fèvre reviewed a series of cases of Perthes disease: 80% had been in boys; the age ranged from 4 to 13 years, with a maximum between 4 and 7 years. He had not found trauma or infection elsewhere to be important antecedents. Pre-existing coxa valga he had sought but had rarely found. He divided cases into two groups, depending on whether changes started in the top of the femoral head or around the margins of the epiphysis. The former he ascribed to interference with the blood supply from the round ligament, the latter to interference with the supply from the circumflex vessels; primary acetabular change might occur also.

Osteochondritis in Congenital Dislocation of the Hip

Dr P. Petit had observed 23 instances of osteochondritis among 87 congenitally dislocated hips. He had not seen a case occurring on the normal side. The prognosis could not be assessed in the first year of life, and in some of the earliest cases there had been complete disappearance of the head. 10 out of 11 cases under the age of 1 year treated by manipulative reduction and fixation in the Lorenz position were complicated by osteochondritis. He reviewed the possible causes of the condition, and suggested that the important factors were (*a*) forcible reduction; (*b*) too powerful traction (the condition is commoner in high dislocations); and, above all (*c*) pressure on the femoral head associated with poor articular contact and torsion of the capsule and its vessels from fixation in the extreme positions. The younger the patient the greater the danger of osteochondritis; the femoral heads of older patients appeared to be more resistant. All cases were due to therapeutic causes, and he recommended reduction by gradual traction with fixation in not more than 60° of abduction, moderate internal rotation, and about 30° of flexion.

Osteochondritis dissecans

Prof R. Guilleminet (Lyons) described 7 cases of osteochondritis dissecans of the hip (Kœnig's disease). Their ages varied from 12 to 51, with most occurring in the 18–25 age group. 5 were male, 2 female. In most there had been no history of trauma, the onset being gradual over the previous six to eighteen months. A few gave a history of sudden "catching" of the hip, but in most the symptoms and signs were those of an osteo-arthritic hip. He had tried removing the affected area, which was always on the top of the head or slightly medial to it, and had even filled the resultant cavity with bone chips, but the results were poor. If conservative treatment failed, arthrodesis was the operation of choice, though one hip recently treated by arthroplasty was still satisfactory. Histologically the appearances were those of a sequestrum; except over the affected area the articular cartilage of the femoral head was normal. Differential diagnosis involved the exclusion of caisson disease, aseptic necrosis from other causes, and tuberculosis.

DISCUSSION

In the discussion Sir Reginald Watson-Jones (London) emphasised that Perthes "disease" was a disorder from loss of local blood supply due to various causes. Rest in bed for two or three years *could* prevent deformation of the femoral head. One must wait at least twenty years to know whether later degenerative arthritis had in fact been thus avoided, but three years' bed rest in childhood was a small price to pay to avert fifty years of later disability which otherwise followed with such certainty.

Prof J. Trueta (Oxford) illustrated the histological and vascular changes in experimental osteochondritis in the rabbit. There was thickening of the epiphyseal cartilage, and vessels could be seen penetrating vertically into the substance of the femoral head, particularly from the outer side. In the man there was no blood supply to the femoral head from the round ligament at the age of 18 months; almost all came from the outer side. At the age of 4 vessels could first be seen entering the head from the round ligament; only after fusion of the capital epiphysis did anastomosis occur between these vessels and the major supply from the outer side, which also supplied the femoral neck; hence the associated changes in this region. After the age of 16 the anastomosis with circulation from the round ligament was adequate and the danger of Perthes disease past. It had been shown by arteriograms that extreme positions of the hip obstructed the circulation to the femoral head.

Mr A. H. C. Ratliff (Edinburgh) gave the results of a late follow-up on 49 cases of Perthes disease, followed for an average period of 17 years. Apart from a few who received no treatment all had been treated by frame fixation. Assessed by a point system relating to pain, degree of activity, range of movement and radiographic appearances they showed 18 good 19 fair 7 poor and 5 very poor results Although [illegible]5% *of the total were still fully active and free from pain* only 38% had good radiographic appearances. Of the 9 untreated cases only 1 had a good hip The most important factor affecting the prognosis was the state of ossification of the head; the younger the child the better the prognosis The average age of onset of the "good" results was 0 of the "fair" 8 of the "poor" 0 and of the "very poor" 10 *Absence of fragmentation was of good prognostic significance* A good immediate result was likely to be maintained for at least twenty five years, even though half of such cases were unsatisfactory radiographically

Dr O Cassucio (Italy) said he preferred the term [illegible]chondrosis. He had done biopsies of capsule cartilage and bone in 18 cases. These showed fibrosis of the capsule *thickening of the cartilage and the formation of an irregular* layer of vacuolated cartilage deep to it which in places had grown down or herniated into the cancellous bone Islands of cartilage were to be found between necrotic bone trabeculæ—an appearance similar to that seen in other osteochondroses The findings were similar to those found in experimental osteochondritis in rabbits All cultures from the biopsy specimens had proved *negative In confirmation of Japanese* work he had found similar changes to follow experimental wounding of the articular cartilage

Arthroplasty in Late Treatment of Congenital Dislocation of Hip

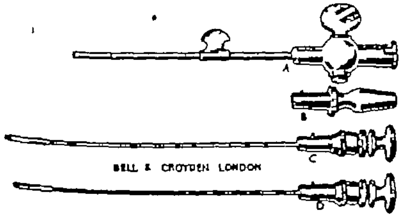
Prof R Merle d'Aubigné (Paris) had done 120 arthroplasties in 90 patients but felt that the indications for any form of arthroplasty should be restricted Arthrodesis was the operation of choice in unilateral cases *only 2 of 17 cases* had been unsatisfactory The Judet operation could give good results but they were too rare In bilateral cases, where *the lesion was asymmetrical* an arthroplasty on the bad side had given poor results in half the cases because of subsequent deterioration in the other hip 12 out of 16 bilateral arthroplasties had been satisfactory Arthrodesis of the more painful side by increasing stability sometimes relieved pain on the other side Resection of the head and neck as in the Girdlestone operation, particularly in those that had had a *previous osteotomy had given very good* results and was also useful where previous arthroplasty with some form of plastic prosthesis had failed After showing *examples of the various groups he concluded by recommending* arthrodesis for the unilateral case and for bilateral cases fusion of the painful side with later arthroplasty or pseudarthrosis on the opposite side if necessary If both sides were stiff and painful at the first examination, then bilateral arthroplasty or resection of head and neck were indicated

New Inventions

ASPIRATION TROCAR AND CANNULA

The disadvantage of the usual trocars and cannulæ used for aspirating fluid from the chest is that, if they are so made as to give a straight run through from cannula via tubing *to syringe* air can enter the pleural space when the trocar is withdrawn and before the aspirating syringe is connected to the cannula. Air may also enter *if attempts have to be made to unblock* the trocar during aspiration Alternatively if the tubing is attached to the trocar by an angled tube obstruction is very apt to develop at the angle and is difficult to overcome during the aspiration

The instrument illustrated here consists of a graduated cannula (11 B.W.G × $2^1/_4$ inches or 14 B.W.G × $2^1/_4$ inches), and a stopcock *with a bayonet* 'Sims' fitting



(A) This connects with a stuffing box and *sharp* trocar (C) a stuffing box and blunt pilot (D) or an adapter (B) attached to a length of rubber tubing which leads to a three-way tap and a *large aspirating* syringe.

With the sharp trocar in position the cannula is inserted into the appropriate intercostal space The trocar is withdrawn To prevent air *entering the stopcock* is closed before the stuffing-box and sharp trocar are disconnected The adapter with the rubber tubing leading to the *three-way tap and aspirating syringe is attached* The stopcock is opened and aspiration is done in the usual way

If the cannula becomes blocked it can be cleared without admitting *air to the pleural space* The stopcock is closed, and the stuffing box and blunt pilot (D) are substituted for the adapter The stopcock is opened and the cannula cleared with the pilot which is then withdrawn The stopcock is again closed while the adapter *is substituted for the stuffing box and blunt pilot* The stopcock is opened and the aspiration continued

These needles are made by Messrs. John Bell & Croyden Wigmore Street London who also supplied the illustration

Brompton Hospital
London

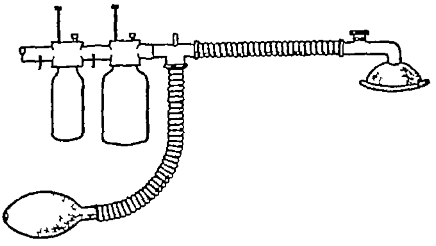
KENNETH ROBSON
M.A., M.D. Camb F.R.C.P.

MODIFIED MAGILL'S ATTACHMENT TO BOYLE'S APPARATUS

This modification allows the anæsthetist to hold the *reservoir bag with both hands for artificial respiration*

Many anæsthetists have for years been using circle absorbers with a length of corrugated hosing leading off to the reservoir bag *This method has the great advantage* that the bag may be held in both hands, and much information may be obtained from it. Artificial respiration is more efficient and *less tiring* with two hands than with one hyperventilation is more easily achieved; the anæsthetist is able to circumambulate in a radius of some five feet round the machine to watch the operation attend to drips, and so on

The same facility may be had with the semi-closed circuit as shown in the accompanying figure Magill's



attachment is modified by interposing a standard length of hosing (from a circle absorber) between the bag mount and the bag *The net physical effect of this* modification is to increase the capacity of the reservoir by about 500 c.c. The behaviour of the circuit is virtually unaltered *once filled with gases it is identical with that* of the unmodified attachment

Nitrous oxide/oxygen anæsthesia with moderate artificial hyperventilation *is greatly facilitated by this* modification

JOHN BULLOUGH
M.B. Lond F.F.A. R.C.S. D.A.
Consultant Anæsthetist
Dartford Group of Hospitals

Reviews of Books

Clinical Diagnosis

ELMER G WAKEFIELD, B S.A , B SC , M D , F.A.C.P , consulting physician, section of medicine, Mayo Clinic New York Appleton Century-Crofts 1955 Pp 1611 $22 50

IT is rare nowadays to meet a large clinical textbook written by a single author Dr Wakefield has tackled his formidable task with courage and energy, and the thoroughness and skill with which he has carried it out are no less remarkable Single authorship gives unity and balance to the contents and style of a book, and it averts repetition—virtues which are seldom evident when there are many contributors and one hard-pressed editor The increasing complexity of medicine has made the single author's task very difficult—but, as this book shows, not impossible It is a considerable tribute to Dr Wakefield's skill and scholarship that it is hard to tell what subjects are his own special field, or when he is drawing, as he must at times, largely on the experience of others

Very little has escaped his net Common disorders are discussed at proper length, and uncommon ones are kept in their right *perspective*, but even the rarest finds a niche somewhere Although his avowed purpose is to consider only the clinical aspects of diagnosis, radiographic, endoscopic, and laboratory methods are briefly mentioned and some indication is given of their comparative usefulness There are also chapters on bodily constitution, the physical effects of environment, and disturbances of electrolyte balance, which are unusual and valuable Dr Wakefield has had the courage and originality largely to discard the customary academic lists of differential diagnoses There are copious references to recent publications in many languages, and though the illustrations are few they are clear and well chosen

The Principles and Practice of Surgical Nursing

D F ELLISON NASH, F.R C S , assistant surgeon, St Bartholomew's Hospital, London London Edward Arnold 1955 Pp 1007 30*s*

NURSES in training are nowadays no less harassed than medical students , and it is alarming that a textbook of nursing concerned only with surgical aspects should run to just over 1000 pages Nevertheless there is no adipose tissue in this book , all its pages are valuable, and some repetition, intentionally introduced for ease of reference, adds little to its weight It is a thoroughly sound and complete work which will undoubtedly find favour as a reference book Mr Ellison Nash has tried to present each subject from first principles and thus avoid a didactic approach and empiricism , and he has succeeded

Graphologie et physiologie de l'écriture

Dr H CALLEWAERT Louvain E Nauwelaerts 1954 Pp 168 $1 80

THE title of his book notwithstanding, Dr Callewaert does not believe that graphology yet exists He has studied by means of cinematographic records the individual movements and postures of writing, which he describes in the first part of the book, and he has acquainted himself with the assertions of the more serious graphologists, which he finds empty of logic and without any statistical foundation Dr Callewaert reviews the anatomical and physiological determinants of script which make it characteristic for the individual, and he draws a sharp distinction between speech, spontaneously acquired by imitation, and writing which has to be learnt by painful labour The constitutional element in psychomotor activity may give an individual imprint to each man's writing, but culture, schooling, and other extraneous influences may also lend the script a deceptive individuality Writing movements cannot be properly equated with expressive gestures for they lack the freedom of choice which the latter enjoy Dr Callewaert, in his just disapproval of the common claims of graphologists, unduly repudiates the expressive and individual quality in handwriting and its potential correlation with personality traits, but his interesting exposé deserves the attention of psychologists and neuropsychiatrists

Clinical Aspects of the Autonomic Nervous System

L A. GILLILAN, PH.D , M D , associate professor of anatomy, Graduate School of Medicine, University of Pennsylvania London J & A Churchill 1955 Pp 316 45*s*

Professor Gillilan, who is an anatomist, gives an excellent and detailed description of the topography of the autonomic nervous system and a full account of what is known of its physiological functions , and the book is valuable for this in itself When it comes to clinical applications, however, he is on less familiar ground, and is sometimes misleading It is, for example, untrue that " digitalis causes vomiting only when the dosage exceeds the therapeutic level " , and to say that " peptic ulcers tend to occur in the slender hyposthenic individual " is ingenuous His enthusiasm for dividing people into vagotonic and sympathotonic types may leave the unsophisticated reader with the impression that the complex interrelationships between mind, personality, body structure, functional order, and disorder are simpler than they really are The text is liberally illustrated by good line drawings

Peripheral Vascular Diseases

2nd ed EDGAR V ALLEN, B S , M A , M D , M S in med., F.A C.P , NELSON W BARKER, B.A , M D , M S in med., F.A C.P , EDGAR H HINES, JUN , B S , M A , M.D , M.S in med , F.A.C.P , professors of medicine, Mayo Foundation Graduate School, University of Minnesota Philadelphia and London W B Saunders 1955 Pp 825 91*s*

BASED on the experience of the senior authors and their colleagues at the Mayo Clinic over the last twenty-five years, this book gives a balanced general picture, and, in addition, sufficient information to satisfy the student interested in the historical development of physiology, pathology, and methods of investigation The first edition, published in 1946, quickly established this as the leading textbook in its field For this edition new subjects, such as aortography, the surgical treatment of aortic aneurysms, and vessel grafting, have been introduced Written with proportion and economy, the text points to the problems still outstanding, but does not leave the reader in a maze of controversy One attractive feature is that each chapter is headed by a photograph and a short biography of a pioneer in vascular work

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Diagnostic électrocardiographique (2nd ed Paris Masson 1954 Pp 448 Fr 4800) —Feeling that the maze of *modern electrocardiography is becoming* labyrinthine in its complexity, Dr André Jouve, Dr Jacques Senez, and Dr Jean Pierron, and their collaborators, have introduced in the second edition of their textbook, the concept of the vectorial loop as a thread to guide the groping student through its mazes No single hypothesis so far advanced, they believe, fully explains the genesis of the electrocardiogram , nor do they accept the vectorcardiogram as such an explanation On the other hand they feel that the vectorcardiogram offers a convenient method of synthesising for the mind's eye the growing number of different electrocardiographic leads currently employed, and that as such it is a useful teaching instrument

The general arrangement of the book is unchanged The first section is devoted to the basic theory and technique of electrocardiography, both of which are handled in great detail, and this is followed by the main section on the normal and abnormal electrocardiogram, considered in relation to alterations in the electrical field of the heart in the body A chapter is given to the arrhythmias, and a short section on clinical applications of electrocardiography ends the book It is profusely, and on the whole clearly, illustrated, though some of the illustrations are overloaded with information (30 leads and 3 vectorial loops are shown in one cardiogram) Moreover, the arrangement of the leads is not uniformly depicted which means that they are often difficult and sometimes unnecessarily tedious to interpret

In its breadth of scope this book is a triumph But a risk is inherent in its catholicism , for in trying to supply the needs of both the clinician and the research worker it may not appeal fully to either

THE LANCET

LONDON SATURDAY JUNE 25 1955

Heroin

THE Government's announcement that after the end of this year the importation of heroin (diamorphine hydrochloride) is to be stopped and its manufacture restricted to small amounts needed for scientific purposes,[1] has been followed by strong protests in the medical and lay press. The ban is being imposed to give effect to a resolution adopted by the Economic and Social Council of the United Nations urging all governments to take this step with the object of checking illicit traffic in the drug. The Minister of Health had previously consulted the Standing Medical Advisory Committee of the Central Health Services Council which endorsed the view that suitable alternatives existed.[2] But on June 3 the representative body of the British Medical Association asserted that the Government could not claim to have consulted the medical profession without having consulted the Association. The representative body was satisfied that heroin should not be exported but called for continuation of its manufacture.[3] The chief arguments adduced in favour of this policy are that in some circumstances heroin is superior to any other drug, that there is little illicit traffic in the drug within this country and no illegal exportation of it, and that a legal ban on the manufacture of heroin can do little good, since this drug is readily made from opium or crude morphine.

Regarding efficacy opinion is by no means united. It seems to be fairly well established that heroin produces greater euphoria with a slighter risk of nausea than an equivalent dose of any other morphine preparation, and some clinicians are convinced that it is sometimes of peerless value—notably in controlling intractable pain and in treating tracheitis. On the other hand, controlled trials comparing heroin with other preparations have been lacking; and as early as 1931 a panel of experts (including the late Prof. W. E. DIXON, of Cambridge) ended its report to the League of Nations with the following words:[4]

> In view of the evidence which we possess, and especially the fact that all the beneficial actions of heroin can in our opinion be obtained by one or other of the drugs mentioned, we believe that heroin can be entirely dispensed with. If the doctors in countries where heroin is used are afforded the opportunity of examining and testing clinically the morphine derivatives to which we have drawn attention, we feel little doubt that they may be induced to dispense with the use of heroin entirely.'

Suppression of manufacture had already been mooted at an international level in 1923 and 1925, but in 1931 the proposal was again defeated, mainly on the ground that the drug was of medical value. But these decisions of course preceded the introduction of synthetic analgesics and of new morphine derivatives.

However much views may differ on the need for heroin to be at the doctor's disposal, we can all agree that in this country nearly all the heroin manufactured is used legally. There are here at present only 54 known heroin addicts, and the Home Secretary is satisfied that there is no substantial hidden addiction.[5] Nor is there any evidence that heroin is being exported illegally. In any case, as Dr D. R. LAURENCE[6] has pointed out, legally manufactured heroin contributes negligibly to the world's illicit traffic. It would, he says, be impossible to control such traffic without control of the illicit traffic in opium and morphine, from which heroin is readily manufactured. Dr LAURENCE's assertion is supported by an official report (1951)[7] that

> reports from governments during the last two years indicated that, thanks to stricter measures of control over manufacture of and trade in heroin put into effect by various governments, diversions from legal into illicit channels due to thefts, robberies, forged prescriptions or laxity in respect of issuance of medical prescriptions have been reduced to the minimum.

And Prof GEORGES BROUET, of Paris, has remarked:[8]

> If morphine continues in current use, heroin is so easy to prepare that there is little point in banning it internationally. If there was any absolute need for prohibiting its use in therapeutics in order to combat addiction, the principle might conceivably be accepted; but if the effect of such prohibition were to be illusory, as we fear it would, it is hard to see why patients who may benefit from it need be deprived of it.'

What then led the Economic and Social Council to make its recommendation? It was acting on a resolution by the sixth World Health Assembly that "the abolition of legally produced diacetylmorphine . . . would facilitate the struggle against its illicit use."[9] Both the Assembly and the W.H.O. Expert Committee on Drugs Liable to Produce Addiction (whose reports were before the Assembly) were impressed by the extensiveness of the illicit use of the drug: in 1951 alone 120 kg. was seized, including 62 kg. in Europe and 26 kg. in the United States.[7] This heroin is believed to have originated mostly in the Far East and on the Mediterranean seaboard. Such traffic can be stopped only by universal enforcement of rigorous measures. At present the countries of the world fall into three groups: (1) those (including the U.S.A.) where all heroin is illicit; (2) those (including Britain and France) where the law seeks to control manufacture and distribution; and (3) those where there is no effective control, and which in some cases export morphine or heroin illicitly on a large scale. Britain's decision to impose the ban can have no direct effect on this traffic; but it might persuade our close neighbour France, which has decided against the ban (and where 1051 g. of heroin was seized in 1951), to reverse her decision. The more countries that impose the ban the easier would be the task of those checking illicit traffic; for wherever the ban operates any heroin found is certainly illicit. Those countries that now act on the Council's recommendation may

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1. See *Lancet*, May 7, 1955, p. 965.
2. *Ibid*, June 18, 1955, p. 12[illegible]1.
3. *Ibid*, June 11, 1955, p. 1220.
4. *Ibid*, 1931, ii, 55.
5. *Ibid*, June 25, 1955, p. 13[illegible]5.
6. *Ibid*, June 18, 1955, p. 1277.
7. *Bull. Narcotics*, 1953, 5, no. [illegible], p. 45.
8. *Ibid*, p. 17.
9. *Ibid*, no. 3, p. 53.

also hope to influence the few countries in the third category—where there is little or no control of production or distribution—to raise themselves eventually to the second or first category Most nations are less insensitive than we sometimes suppose to the climate of opinion around them , if only one or two isolated countries were left trafficking freely in heroin the weight of world opinion might lead them to re examine their practice By now imposing the ban Britain is making her own small contribution to this end

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Cobalt and Anæmia

COBALT deficiency is known to occur in sheep and cattle in Denmark, Australia, and some other places where the soil and grass are deficient in this element The syndrome, which has various local names, such as " bush sickness," is characterised by some anæmia, and by poor growth, lack of appetite, and emaciation[11] The fact that vitamin B_{12} contains 4 5% of cobalt shows that cobalt is necessary for normal nutrition in man as well , but since the daily requirement of vitamin B_{12} in man has been put at no more than 1 µg , cobalt can properly be regarded as a " trace element " Cobalt has been used for the treatment of anæmias which are refractory to the normal hæmatinics, especially iron , such anæmias develop in chronic infections, after burns, in kidney disease, and in some children Compared with the daily requirement of about $^1/_{25}$ of a microgramme the doses of 20–60 milligrammes daily of cobaltous chloride (about 9–25 mg of cobalt) that are given therapeutically are relatively enormous, and it is clear that any action cobalt has on refractory anæmias must be quite different from its physiological action

WINTROBE and his co-workers[12] produced local inflammation in rats with turpentine and showed that the consequent anæmia could be overcome by giving cobalt salts They were surprised to find that polycythæmia was induced in these animals, and further work[13] showed that the absorption of iron from the alimentary tract was increased by giving cobalt Later work suggested that daily doses of up to 100 mg of cobaltous chloride given to patients with anæmia associated with chronic infections produced a reticulocytosis in about six days and an increase in the circulating red cells and hæmoglobin , but, judging by the few reports published in the past five years, this treatment has not been widely applied in practice

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COLES[15] has reported results with cobalt treatment of some of the anæmias of childhood Altogether 50 patients were treated In 31 the anæmia was associated with infection, 10 were anæmic premature infants, n 3 the anæmia was due to rhesus incompatibility and the remainder were a miscellaneous group COLES states that these types of anæmia usually respond poorly to iron, liver, and other hæmatinics but she describes no evidence that these particular 30 patients were in fact refractory The infections that caused anæmia were predominantly otitis media and bronchopneumonia, and the blood picture was normochromic COLES does not give individual counts, but only average figures on which it is more difficult to judge the value of the treatment Most of the patients received 25 mg of cobalt sulphate daily for three weeks, and no toxic effects were noted The average rise of hæmoglobin was from 9 23 g per 100 ml to 11 24 g per 100 ml and the greatest rise occurred in the first week. The 9 premature infants received 20 mg of cobalt sulphate daily for three weeks, the average hæmoglobin level rose from 9 17 g per 100 ml initially to 12 28 g per 100 ml, again with the greatest increase in the first week The other patients also responded satisfactorily Cobalt was also given to a child with a chronic hypoplastic anæmia who was being treated with repeated blood transfusion there was no response—which agrees with the experience of most others COLES examined the bone-marrow before and after cobalt treatment in 12 patients There was an increase of erythropoietic cells in all, in the patients with infections the increase was mostly in the pro-erythroblasts and the earlier normoblasts whereas in the premature infants the later normoblasts were most increased. COLES suggests that this denotes that cobalt has a different action in the two groups in the premature infants iron supplies are adequate and cobalt enables the erythroblasts to utilise iron more efficiently in the anæmia of infection cobalt directly stimulates erythropoiesis in a previously depressed marrow

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[10] Eddy N B *Ibid*, no 2 p 39

[11] Underwood E J *Nutr Abstr Rev* 1940 9 515

[12] Wintrobe M M, Grinstein, M , Dubash J J Humphreys, S R., Ashenbrucker H , Worth W *Blood*, 1947 **2** 323

[13] Gubler C J Cartwright G E Wintrobe, M.M. *J biol Chem* 1950, **184** 575

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All these reports will encourage further trial of cobalt in the treatment of patients with these anæmias that respond poorly if at all, to the usual hæmatinics, who usually have to be treated by repeated transfusions But two warnings must be given In the first place it is desirable that patients with these refractory anæmias should receive cobalt therapy early in the course of their disease the value of treatment with cobalt is not easily assessed when it follows soon after a course of blood transfusions, the exhibition of cortisone or splenectomy In the second place in the dosage used cobalt can have unpleasant toxic effects The immediate effects such as nausea vomiting, and anorexia, can be averted by using enteric coated tablets Some patients have unpleasant tinnitus or flushing of the face[14] A more serious goitrogenic effect has been reported.[18] KRISS et al were administering enteric coated tablets of cobaltous chloride in doses varying from 30 to 100 mg daily for the treatment of sickle cell anæmia Goitre and hypothyroidism developed in 2 of their patients, in one treatment for myxœdema was needed, and in the other the thyroid tumour appeared clinically to be a carcinoma They found 3 other cases of thyroid hyperplasia by examining post mortem tissues The explanation of this action is uncertain. It is known that cobalt given in doses larger than those administered clinically, can cause polycythæmia in rats It seems to be agreed that this action is due to anoxia from inhibition of some of the enzymes concerned with the transport of oxygen, thus LEVY et al[19] found that cobalt inhibited two sulphydryl dependent enzymes—succinic dehydrogenase and choline oxidase The erythropoietic stimulation may therefore be a response to a toxic anoxæmia The goitrogenous action noted by KRISS et al may be due to interference by cobalt with the enzyme system that forms mono-iodotyrosine If the stimulating' action of cobalt on erythropoiesis in refractory anæmias depends on its toxic properties, then it should clearly be administered cautiously and should not be included in iron or other preparations for the treatment of anæmia Like all other hæmatinics, it should be given alone

Annotations

CANCER OF THE LARYNX

IN the past it has been very difficult to assess the results of different forms of treatment for cancer of the larynx This was due partly to the relatively small number of cases in individual series but very largely to differences in definition classification and grading of the tumours In the past decade or two there has been a growing tendency to centralise the management of these relatively uncommon tumours and laryngologists and radiotherapists are slowly approaching unanimity on classification and grading In the past three months three large series of results have been published in which the classification was the same

Growths of the laryngopharynx were previously known as extrinsic laryngeal cancers now they are described by most laryngologists as cancers of the pharynx Anatomically they belong to the pharynx clinically they behave quite unlike the true laryngeal growths They produce symptoms late they metastasise early to the regional lymph nodes, they respond very poorly to any form of treatment and they have a most depressing prognosis The term laryngeal cancer is now usually limited to those growths which were previously known as intrinsic or endolaryngeal cancers Most of these produce symptoms early metastasise late are eminently treatable and have a much better outlook Indeed in the case of early carcinoma of the vocal cords the prognosis is better than with cancer at any other site.

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[16] Seaman A J, Koler R D *Acta hæmat* 1953, 9 153.
[17] Fountain, J R, Dales M *Lancet* March 12, 1955 p 541
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[19] Levy H Levison V Schade A L *Arch. Biochem* 1950 27 31
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[19] Levy H, Levison V Schade A L *Arch Biochem* 1950 27 34

[20] Nielsen J, Strandberg O *Acta radiol Stockh* 1942 23 189

In *stage 2* the tumour involves the anterior commissure and, perhaps a greater or lesser part of the anterior two thirds of the true vocal cord The mobility of the cord is still unaffected

In *stage 3* the tumour extends beyond the vocal cord, which is more or less fixed Involvement may be unilateral or bilateral The lymph nodes, however, are not affected

In *stage 4* the tumour extends beyond the larynx, commonly with lymph node involvement

Falbe Hansen,[21] of Copenhagen, describes the results of surgical treatment of laryngeal cancer Operation is indicated, he says, in subglottic cancer and in cancer of the vocal cord with complete or almost complete fixation It is further indicated where a "test treatment" with radiotherapy has shown no effect, and in cases of residuum or recurrence after such therapy 38 laryngectomies were done between January, 1942, and January, 1949, with a minimum follow up period of five years 35 of the patients were men only 3 women Of the 38 cases, 36 belong to the 3rd or 4th stage In each of the 2 cases in stage 1 or 2 there had been a recurrence after radiotherapy Five years or more after laryngectomy 21 of the patients—55% of the total—were alive and well, 6 other patients had died from other causes, without signs of residuum or recurrence, less than five years after operation The lymph nodes were removed, together with the larynx, in 7 patients with stage 4 cancers 1 of them died fifteen days after the operation from severe sepsis, and recurrences developed in 2, but 3 were alive and well at the end of six to eight years, and 1 died of appendicitis seven months after operation, without any signs of recurrence Preoperative radiotherapy was given in 14 cases, and 9 of these patients are alive and symptom free after more than five years, while 4 have died, without any sign of recurrence, at various intervals after the operation These results are impressive

Wang and O'Donnell,[22] two radiotherapists at the Massachusetts General Hospital, record the results in 253 cases of cancer of the larynx, with the emphasis on radiotherapy These patients were treated between 1931 and 1949, again with a minimum follow-up period of five years They advocate tomography and lateral soft tissue radiography for determining the extent of the tumour 95% of their patients were men Of 35 patients stage 1 growths treated by radiotherapy, 80% were symptom free after five years, of 15 patients treated by surgery, 86% were alive and well

Of 19 patients with stage 2 growths treated by radiotherapy, 68% were alive and well after five years, of 12 patients treated by surgery, 58% survived Of 58 patients with stage 3 growths treated by radiotherapy, only 24% survived for five years, no less than 53% of those treated surgically survived for the same period Of 46 patients with stage 4 growths treated by radiotherapy, 15% were free of recurrence five years after treatment, of 7 patients treated surgically, 13% survived

Nielsen[23] believes that the main problem in the treatment of these tumours centres round coöperation between surgeon and radiotherapist, to obtain "the highest numbers of cures with the maximum of functional results" At the moment, he says, opinions seem to vary between the two extremes of 100% surgery and 100 % irradiation Nielsen, a radiotherapist, has collaborated with Falbe Hansen, his laryngologist colleague, in treating his cases Since 1942 all stage 1 and stage 2 cases have been referred primarily for radiotherapy, the majority of stage 3 cases have also been primarily irradiated, except for subglottic cancers and cancers of the vocal cords with complete or almost complete fixation, primary irradiation was preferred in stage 4 cancers arising from the subglottic region Of the 235 patients in this series the majority were treated by radiotherapy In the two earlier stages about 80% survived for five years after radiotherapy, and a further 10% died from another cause before the five-year limit Of 18 cases of subglottic cancer, a third were cured by surgery, and only 1 single case by radiotherapy

Several points emerge from these three large series, amounting to over five hundred cases assessed by one classification In cases of early cancer of the true vocal cord, without limitation of mobility, the results of radiotherapy differ very little from those of surgery in terms of life and "five year cures", but the functional results, as regards the voice, are much better with radiotherapy "In this respect I think most laryngeal surgeons are agreed," says Falbe Hansen, but, he adds, "only very few seem to act accordingly" Surgery alone gives incomparably better results than radiotherapy alone in stage-3 growths which have infiltrated the vocal cords or extended beyond them, yet are still within the confines of the larynx But, as Wang and O'Donnell say, since a quarter of stage 3 growths can be controlled by radiotherapy, with preservation of voice, "a fair trial of this conservative method should be carried out If the tumour does not respond favourably to radiation, total laryngectomy may still be done" Mono block dissection of larynx and glands will probably be practised more commonly in the future in stage 4 growths, and even better results will be obtained in these more advanced tumours by a formal combination of radiotherapy and surgery As in other aspects of otolaryngology, the emphasis is shifting to preservation of function

HYPOPHYSEOTOMY IN DIABETES

In young adults with "malignant" diabetes, for whom nothing but further deterioration can otherwise be expected, Prof H Olivecrona and his colleagues in Stockholm have obtained considerable improvement by removal of the pituitary gland [1]

In the Ciba Foundation lecture, written with Dr Rolf Luft, which he gave in London on June 15, he explained that this work, starting in 1951, was based on experimental evidence of the diabetogenic action of growth hormone and adrenocorticotrophic hormone,[2] and on reported regression of diabetes in several cases of pituitary deficiency So far, he has operated on 17 patients, all with advanced diabetic retinopathy and all with renal damage in some degree—often far advanced Of the 3 operative deaths 2 were from complications such as may follow any major operation, and it should be remembered that the juvenile diabetic with vascular disease is not a good subject for surgery Of the 4 patients who have died since leaving the clinic (2 of them surviving eighteen months), 3 were treated too late to derive substantial benefit The remaining 10 patients are alive after periods ranging from five months to three and a half years, during which they have had substitution therapy with cortisone, thyroxine, and (in most cases) testosterone or stilbœstrol, together with smallish doses of insulin Up to date, the eye ground changes appear to have been arrested exudates have decreased or remained stationary, proliferation of blood vessels is no longer progressive, and hæmorrhages have slowly disappeared, though new ones have occasionally been observed in the first few months In every case, except 1 in which hypophysectomy was incomplete, renal blood flow has increased or remained stationary, and of the 8 patients who had arterial hypertension all now have blood-pressures within normal limits From this preliminary assessment of hypophysectomy as a means of preventing blindness and irreparable renal damage "we think that our results are encouraging" said Professor operations Better results, he believes could be expected if the operation were carried out earlier

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[21] Falbe Hansen J *J Laryng* 1955 69 255

[22] Wang C C O Donnell A. R *New Engl J Med* 1955 252,743

[23]. Nielsen J *J Laryng* 1955 68 370

[1] See *Lancet* 1954, ii, 700

[2] *Ibid*, 1952 i 35

Prof C H Best F R.S presided at the lecture and a vote of thanks was proposed by Lord Adrian F R.S who expressed lively interest in what he regarded as purely a development of neurosurgery

ANGIOCARDIOGRAPHY IN CHEST DISEASE

It might have been thought that angiocardiography would prove of great value for investigating pulmonary disease, but so far this application has been comparatively limited. Abels[1] now describes angiocardiographic studies in cases of pulmonary and mediastinal abnormalities discovered in mass-radiography surveys Of the 12 illustrative cases that he cites 4 had lesions in the lung fields, and in 3 of these a presumptive diagnosis of arteriovenous aneurysm or hæmangioma was confirmed by displaying the vascular tree Tomography as Abels points out is very helpful in such cases since it often shows vascular tufts associated with the lesions The fourth pulmonary lesion was a curvilinear opacity near the heart shadow which was shown to be an anomalous pulmonary vein In the other 8 cases radiographs of the chest showed mediastinal or paramediastinal abnormalities and in this type of case as Abbott et al[2] had previously found angiocardiography was of more decisive diagnostic importance suspected vascular lesions were accurately localised—for example a putative aortic aneurysm was proved to be an aneurysm of the pulmonary artery and a thymoma associated with a systolic murmur was demonstrated before operation not to be a lesion of a great vessel

The scope of angiocardiography in diseases of the chest may be extended in the future. Cudkowicz and Armstrong[3] have reported differences between the vascular patterns of primary and of secondary neoplasm and Sleeser et al[4] have averted fruitless thoracotomy in some patients with bronchial carcinoma by demonstrating neoplastic involvement of the great vessels But, as Abels points out, angiocardiography is not without risk. It should be undertaken only where it seems essential in order to establish the diagnosis.

DELIVERY BY SUCTION

In the past many ingenious and elaborate obstetric forceps have been devised—one of these was so complex that a screwdriver for running repairs was included in its handle Nowadays forceps are lighter and shorter Even the axis traction instrument devised by Tarnier and so beautifully worked out mathematically by Milne Murray is no longer necessary now that the high forceps operation is rarely practised It is generally agreed that if more than gentle traction is necessary this usually indicates that the time or method of delivery has been misjudged For the simple low extraction Wrigley's forceps have become popular and Finderle[5] describes an even lighter implement which can be applied to the vertex by suction. It consists of a horn shaped cup which at its wider end is covered by rubber and at its narrow end is attached by tubing to a syringe. The position of the head is determined and the wide end of the horn is introduced through the introitus and applied to the head A partial vacuum is created by two or three thrusts of the syringe and maintained by a stopcock. There are light metal finger rests on the narrow end of the horn and by traction on these the head is delivered

Finderle states that in the last 4000 or more deliveries at his clinic the use of forceps has been completely discontinued He reports 132 successful extractions 103 of the patients were primigravidæ, and the majority of the babies were mature and of average weight There were no deaths or complications attributable to the extractor and from the information that the use of forceps has been discontinued we must conclude that there were no failed extractions Sometimes an artificial caput succedaneum has formed on the baby's scalp but this has always disappeared within a few hours. The level of the head at delivery is not specified, but the cæsarean section rate at the clinic is only just over 2% so apparently the use of the extractor is not confined to cases in which the head is on the perineum Anæsthesia has not always proved necessary, but episiotomy under local anæsthesia is usually done in the primigravida before the extractor is applied Finderle claims that the head can be readily rotated by means of the applied horn and he also reports 4 successful applications to the breech

It is unlikely that this instrument (which resembles others previously devised) can completely replace the forceps but Finderle's results suggest that its value should be further tested.

A NEW ENTERIC ORGANISM

THERE is much to be said for the suggestion by Edwards and West[1] that the enteric bacteria should be regarded as a continuous series of interrelated types rather than be classified in rigid groups such as salmonella arizona and paracolon ' While some—e.g , *Salmonella typhi* or *S typhimurium*—have reasonable claims to be regarded as species since they are fairly constant in habit in vivo and in vitro and are readily distinguished from related organisms, we should remember that they owe their places as ' type specimens to their common occurrence as parasites of man in the temperate zone. Deliberate search and chance observation have now raised the number of more or less typical members of the salmonella group to about 300 and at the same time have yielded strains which have some but not all of the biochemical and antigenic characters typical of Salmonella Many such are probably overlooked for obvious reasons some are found once only studied in some detail and then put aside in case another turns up It seldom does and for this reason a paper by McDonald et al[2] is of interest Since the end of 1951 strains of ' atypical paratyphoid bacilli ' have been reported from places as distant as Inverness and Newport, Mon They have been isolated from 99 people of whom 43 had acute gastro-enteritis and the rest no symptoms at all. Most of the infections were single but a small epidemic in Gateshead involved 14 people[3] The organism presumed to be responsible differs from *S paratyphi B* in that it fails to ferment dulcitol cannot be typed by bacteriophage and has the antigenic formula IV V XII b :—(*instead of* I IV V XII : b : 1 2)

The distinction of infections due to this organism from paratyphoid fever may be of administrative importance. As Savage pointed out,[4] many infections with *S paratyphi B* cause only an acute enteritis with a short incubation period The responsibility for differentiating infections by the enteric group of organisms must lie with the laboratory and this paper is a good advertisement for the Salmonella and Enteric Reference Laboratories Few diagnostic bacteriologists are adepts at the finer points of antigenic analysis or bacteriophage typing The reference laboratories not only afford these services to all but are best placed to observe the changing prevalence of bacterial species and the emergence of types not seen before It would be nice to know how often in the past this new organism has been called a paratyphoid bacillus That it is a cause of human illness we have little doubt, and it may be found to have an even wider distribution Whether it is labelled *S paratyphi B var*, or *S java* (which it seems to resemble), or "paracolon" is unimportant (except to the systematists) now that occurrence and identity have been recorded It matters more that all should realise that the ability to cause disease is not limited to organisms in the Kauffman-White list of salmonellæ

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[1] Abels E. V F St J Med, 1955 85 1450
[2] Abbott O A Hopkins W A Leigh T F J thorac Surg 1949 18 569
[3] Cudkowicz, L. Armstrong J B Thorax 1953 8 152
[4] Sleeser B.V Britt R. G Freer J L Ibid 1954 9 91
[5] Finderle, V Amer J Obstet Gynec 1955 69 1148

[1] Edwards, P R. West, M G J infect Dis 1950 87 184
[2] McDonald, J C., Price A Taylor J Mon Bull Minist Hlth Lab Serv 1955 14 83.
[3] Grant J Morton R. Ibid p 97
[4] Savage W J Hyg Camb 1942 42 393

It would indeed be remarkable if pathogenicity were associated quite strictly with biochemical habit or antigenic structure Two of the more successful and specialised parasites—*S typhi* and *S pullorum*—are both nonconformist in vitro Until we know far more than at present it will be wise to regard all the organisms which share the major antigenic factors and some of the biochemical habits of salmonella as potential agents of disease

IMMEDIATE DENTURES

THE Ministry of Health memorandum to local authorities which we summarised last week, gave some depressing figures to show how much money had been spent on dentures during the first five years of the National Health Service The total was about £100 million, and, if the present demand is maintained, it is likely that, in a few years' time 1 in 6 of the population will wear dentures, and two fifths of them will be under 45 We cannot, of course, know how much of this prosthetic work was avoidable, or just how many sets of teeth have been ruined by neglect, but it is plain enough that the dental health of the nation is far worse than it should be Energetic propaganda by both doctors and dentists is undoubtedly part of the answer, but, however effective that may be, we shall still have to provide for the edentulous patient for many years to come

By means of acrylic resins, dentures can now be made far more pleasing æsthetically than when they were made in vulcanite, but patients are understandably becoming more exacting, and a denture is expected to reach a high standard in comfort and efficiency as well as in appearance As Gimson[1] points out, many of the difficulties of constructing full dentures are the result of leaving the patient edentulous for the customary time of three to six months Immediate dentures have many advantages, apart from the obvious one of escaping the toothless weeks after extractions Anatomical changes in the temporo mandibular joint and in the shape of the tongue are avoided, and there is no opportunity for the patient to learn incorrect habits of mastication, nor for the facial contour to collapse The task of the dental technician is made easier, for the natural teeth, or an impression of them, can be used as a guide to the occlusion and, if necessary, to the shape and position of the teeth

Various techniques may be followed, but one which gives good results is to extract the posterior teeth first, and then, after a lapse of six to eight weeks, so make a partial denture After a further period of a week or two, the anterior teeth are extracted and the denture completed This is quite satisfactory provided that the patient understands that it will be necessary to have the dentures relined after three or four months, and provided that certain precautions, as outlined by Gimson, are taken An alternative method, perhaps rather more popular in the United States than in this country, is to perform an alveolectomy when the anterior teeth are extracted This has advantages when the natural incisors are unduly prominent because of malformation of the pre maxilla, and it also makes it possible to fit a labial flange to the upper denture But the nervous patient does not always like the extra operation, and it is perhaps better to reserve alveolectomy for those in whom a good cosmetic and functional result could not be obtained by simpler methods

When an upper immediate denture is made without an alveolectomy, it is usual to "socket" the artificial teeth, and it is at this stage, Gimson emphasises, that considerable damage may be done to the ridge There is a temptation to fit the artificial roots well up into the sockets, probably in the hope that when absorption is complete the denture will still be a reasonable fit Unfortunately what happens is that at the end of seven or eight weeks, the ridge shows deep and permanent cavitation and is anything but suitable as a stable base for a denture Gimson describes the technical details necessary to ensure a correct fit for the anterior teeth —but, as he is careful to stress, it is essential to make regular adjustments to the denture as absorption proceeds A new denture will probably be needed in anything from six to twelve months after the insertion of the immediate denture For success, the patient's cooperation is essential, he must be prepared to return frequently for adjustments, and the dental surgeon must realise how vital these adjustments are

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[1] Gimson, A P *Brit dent J* 1955 98, 387

RECONSTRUCTION OF HAND DIGITS

RECONSTRUCTIVE surgery of the hand is applied to two broad groups of patients—those with congenital deformities, and those with mutilated fingers The former group often have associated malformations, but show considerable adaptive powers which may make reconstruction unnecessary or undesirable Most of the operations designed to replace or refashion digits depend on the use of structures in the hand itself, but several attempts have been made to use the toes to repair a defective or damaged hand Esser and Ranschburg[1] have described a successful graft of four toes to a hand. Blair and Byars[2] and Young[3] have each described single cases of a finger successfully reconstructed with a toe, while a less successful case has been reported by Neuhof[4] Clarkson[5] has developed this technique, mainly for thumb defects A dorsal flap is made on the foot, extending proximally almost to the ankle joint, and is delayed in one or two stages The hand is prepared by creating a matching skin defect, and is brought down to the foot The foot tendons are divided in the ankle region, and are sutured to those in the hand The skin flap is then sewn in place Six weeks later the toe is amputated through the metatarsophalangeal joint, and the wound is covered by grafting The new thumb may be modelled as necessary In Clarkson's patients nerve suture has not been performed It would be useful to know the amount of sensory perception in the new digit Bunnell[6] condemned this type of operation where there was subsequently no reliable tactile and proprioceptive sensation Nevertheless, the foot-to-hand graft may be of great value to patients in whom local operations are impracticable

On June 20 the DUKE OF EDINBURGH was installed as an honorary fellow of the Royal College of Surgeons of Edinburgh which is celebrating its 450th anniversary

The Medical Disciplinary Committee of the General Medical Council will meet on Tuesday, July 12, at 10 30 A.M

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1 Esser J F S Ranschburg P *Ann Surg* 1940, 111, 655
2 Blair V P, Byars L T *Ibid* 1940 112, 287
3 Young F *Surgery* 1946 20 117
4 Neuhof H *Ann Surg* 1940, 112 291
5 Clarkson, P *J Bone Jt Surg* 1955, 37A, 270
6 Bunnell S Surgery of the Hand London 1948

Special Articles

DISPOSAL OF THE CHRONIC CASE

J. R. D. BAYNE
M.D. McGill
SENIOR HOUSE-OFFICER

MARJORY WARREN
M.R.C.S.
CONSULTANT PHYSICIAN

GERIATRIC UNIT, WEST MIDDLESEX HOSPITAL, ISLEWORTH

In modern medical practice suffering tends to be reduced to a mathematical equation. We speak of morbidity and mortality rates, incidence of disease and survival time. Assessment of disease in these terms gives direction to further study and indicates its urgency. But there is a danger of mistaking a calculated solution for a remedy, forgetting that finally we are treating not a disease but a person. To speak of the "disposal" of patients suggests that the danger is real.

Yet a hospital unit or firm may say that if the chronic cases could be disposed of there would be room for all the acute cases, and that the need today is for chronic hospital beds. The implication is that these patients are beyond further therapy and can never return to their home community. If it is held that no therapy is needed the medical staff of a chronic-sick hospital should be small. The medical officer would be expected merely to look after the patients in any acute intercurrent illness. No patients would be discharged.

But who decides that a person is irremediable and beyond therapy? Will the decision be based on the knowledge that this type of case is hopeless, or that this particular patient has not responded? If new therapeutic methods offer new hope, who will review the case? And what will be the possibility of the patient gaining reassessment if he asks for it?

The following case-history is an example of what may occur. It offers no new therapeutic method, no tit-bits of pathogenic mystery, yet it deserves the attention of the busy physicians who every day dispose of chronic cases and sometimes may unwittingly add misery to suffering.

CASE HISTORY

In July, 1954, the geriatric unit was asked by the regional hospital board to accept a case of long-standing hemiplegia from a chronic-sick hospital in the provinces which was closing for repairs. The patient's home was believed to be at Twickenham, Middlesex. She was admitted on July 28. A brief accompanying letter said: "She has been bed ridden for years due to left hemiplegia and mentally is still unstable."

The patient was 74 years of age, and able to give a clear and consistent history. She said that until she was on the train she did not know to where she was being moved. She was born with a left-sided weakness and shaking of the left arm. Her two sisters and three brothers were normal. They regarded her as likely to be a burden on them and she determined to be independent. At the age of 16 she entered domestic service and became self-supporting; later on she rented a room and worked as a charwoman. She was able to get about without sticks and to climb the two flights of stairs to her room. She never moved from London. After her mother's death in 1923 she became gradually estranged from her relatives.

In 1925 she entered hospital for the first time because of an attack of influenza. She was persuaded to accept surgical treatment for her deformed left foot, but it was not a success and the wound did not heal. She continued to work, but it became difficult to find jobs because of her disability and local sepsis. In 1935 she re-entered hospital for treatment of a chest infection and on recovery she was advised to accept amputation of the foot or leg. She refused and was not given her discharge because her leg was regarded as "a danger." Her room was given up and her personal belongings scattered.

In 1940, when the chronic sick were evacuated from the bombing areas, she was transferred from London to a chronic-sick hospital in the provinces, where she remained until 1954. She asked repeatedly if she might get up, but was not allowed even to sit in a chair until lately. The following excerpts from the scanty records, which were sent complete with her, are typical:

1942.—She was seen five times and noted as being in satisfactory condition "and her speech intelligent."

1943.—She had a "violent hysterical attack."

1948.—She was treated with tincture of stramonium.

1949.—There were trophic changes of the feet with bilateral foot-drop.

1950.—A complete re-assessment was carried out by a consultant physician interested in rehabilitation. He wrote:

> Her mental processes are very unstable. Liable to hysterical attacks and aggressive towards patients at times. For this reason improvement of her spastic state by rehabilitation unlikely.

In the next two years she had two more outbursts of hysteria, and she was twice treated with antibiotics for respiratory tract infection. Short notes were made at three-monthly intervals up to her transfer to the West Middlesex Hospital.

On examination she was alert, rational, coöperative, and correctly oriented. Her memory for distant and recent events was good. There were no delusions or hallucinations. She was neat and tidy in appearance. The chest and abdomen were normal. The pulse was regular; there was a systolic murmur at the apex and splitting of heart-sounds at all areas; blood-pressure 140/80 mm. Hg; electrocardiography showed a right bundle-branch block. The skin of both lower legs was thin, pink, and shiny, and they became cyanosed on dependency. The left ankle was fixed in equinus deformity. Radiography showed a varus deformity of the left hip suggestive of congenital dislocation of the hip; the pelvis was asymmetrical, and there were osteoporotic changes in the left ankle. There was divergent strabismus with impaired vision of the right eye. Spastic weakness of the left arm and leg with a coarse flapping tremor of the left arm were present. Hæmoglobin 14.4 g. per 100 ml. (97%) and blood Wassermann reaction negative.

She was given clothes and was able to dress at once. Oversize shoes were put on her feet and she was soon able to walk between parallel bars. The orthopædic surgeon then performed a wedge tarsectomy of the left foot. The compression clamps were removed and a new plaster cast applied three weeks after the operation. She tried to walk with a crutch and holding a handrail but was handicapped by her weak incoördinate left arm. Two months after the operation she was given a walking plaster cast and soon could walk pushing a chair. She practised constantly by herself and refused unnecessary help if offered. When the cast was removed, surgical boots were fitted with a small heel raise on the left boot. She walked with a stick and went up and down stairs unaided. During her stay in hospital she was given new glasses, new dentures, and new clothes. She was interviewed by a welfare officer of the London County Council (since she was never a resident of Middlesex) and accepted by him on Feb. 28, 1955, for a welfare home in the vicinity of her old home. She thus returned after twenty years in hospital and thirty weeks of active treatment.

DISCUSSION

We have related this case-history not to elicit praise for any unit or therapeutic method, or to blame physicians for any lack of interest or treatment. The patient herself says she was treated with great kindness and the record shows no blemish. But we must criticise the negative therapeutic approach that cost the patient twenty years of freedom. Such an attitude is almost inevitable when patients are not seen until they have substantially lost their independence and have become bedfast. Only those who watch the decline from the first stages will appreciate the lost opportunities.

As this case-history shows, even review by a physician skilled in rehabilitation could not undo the psychological adhesions that bound the patient to bed. Yet all that was required finally was encouragement and a positive approach. Mistakes of this kind will not be avoided by the review of patients in chronic sick hospitals, but only by their repeated review in a long-stay annexe. Whenever possible the annexe should be an integral part of the unit to which they first appealed for help.

TREATMENT CENTRE FOR ALCOHOLICS IN A MENTAL HOSPITAL *

M M GLATT
M D Leipzig, D P M
SENIOR HOSPITAL MEDICAL OFFICER, WARLINGHAM PARK HOSPITAL, SURREY

IN 1948 in England and Wales the number of alcoholics with complications ("chronic alcoholics") was estimated at 86,000 (Jellinek 1951) This estimate was based on the percentage contribution of alcoholism to the number of deaths from liver cirrhosis Deaths from liver cirrhosis have risen from 816 in 1948 to 1155 in 1953 (Registrar-General 1949–54), and the W H O Alcoholism Subcommittee (1952) has suggested that this increase reflects an increase in the rate of alcoholism In view of the dearth of facilities in this country for the treatment of alcoholics (Dent 1952, Pullar Strecker 1952, 1955), the following description of a treatment programme evolved by trial and error at this public mental hospital may be of interest

The Start

Our first alcoholic group was formed in August, 1952, when four alcoholics happened to be in hospital at the same time These patients felt that they derived benefit from the group approach, and gradually the number of meetings and of alcoholic admissions increased To start with the group only met for an hour twice weekly, meetings are now held daily, and the male alcoholics form a closely knit, well organised group who live together in a ward, where they form at least half of the ward population, work together in occupational groups and usually also take recreation together (Glatt 1955)

The popularity of the group meetings in the hospital gave rise to the idea of forming similar groups for alcoholics after discharge and for outpatients At first there were not enough ex-patients to form such groups and there was no branch of Alcoholics Anonymous in our catchment area Our hospital group was therefore used as a nucleus to form a new A.A group at Croydon, which, with the help of the London service office of A.A , was started in November, 1952, and grew rapidly through the influx of non hospital alcoholics from the district All the Croydon A.A meetings, as well as those of other A A branches in the neighbourhood, have since been regularly attended by our hospital patients Two years ago they also formed their own A.A group in the hospital, and they hold open meetings every Sunday evening These meetings, as well as a Sunday afternoon meeting held by the social worker, give visiting relatives a chance to gain insight into the problem

Former patients have a standing invitation to attend hospital group meetings after discharge, and to keep in touch with ex patients who live in other parts of London Monthly reunions have been held in London for over a year Reports of these meetings are mailed regularly to all our alcoholic ex-patients, and have gradually expanded into a typewritten monthly magazine of 30–36 pages, now in its second year

Treatment

Sobering-up, detoxication, and physical building-up are no more than preliminary stages in the treatment of alcoholism Our long-term treatment programme for alcoholics is based on community living with other alcoholics, group therapy, close collaboration with A A., the use in some cases of drugs—such as disulfiram ('Antabuse') and apomorphine—as auxiliary weapons, and keeping in contact with patients after discharge

Community living and group therapy appear theoretically to be suitable means of treatment, for group activities seem to be a natural antithesis and antidote to personality traits often found in alcoholics, such as defiant individuality, grandiosity (Sillman 1948, Tiebout 1949), undersocialisation, and underparticipation in the activities of their surroundings (Bacon 1949) In a community and in groups formed by alcoholics who all speak the same language—enabling rapid identification with each other—each soon gets the feeling of belonging and learns to give up individualistic striving for the sake of sharing in the work for a common goal Each helps others by trying to help himself, and he gets encouragement to drop his façade and to reveal and face his real self when he sees others do it Often the alcoholic has been driven to drink because he felt unable to form human relationships without it, finally he has withdrawn more and more from society because of drink Community living and group activities help him in the process of resocialisation

In each patient alcoholism is probably due to severa causes, and no single form of therapy is suitable fo every patient A combination of several therapeutic methods selected according to the needs of each patien seems to be the most promising way of treatment Group therapy has been chosen here as the centra line of approach, for it makes the patient himself a active participant and is carried out with, and to a larg extent by, the patient himself and is not merely a therap meted out to him

The method used in the group discussions is in the mai a form of eclectic psychotherapy based on dynam concepts and a predominantly non directive approach Emotional reorientation and not mere intellectua understanding is the chief goal

Meetings are attended by doctors, the hospital chaplain —spiritual subjects often crop up at group meetings o alcoholics—and social workers, but they may also b held when no members of the staff are present

Aftercare

As the success of treatment of alcoholics rests largel on the standard of aftercare, we do our best to establis good contact and rapport with patients and their relative before discharge, and to anchor the patient firmly i A A On an average 10 patients—unaccompanied by hospital staff—visited outside A A meetings twice a week for over two years, and only rarely did any of them absent himself for a drink This may be partly due t the absence of responsibilities while in hospital, but i probably also due to the patients' acceptance of th code of their hospital group, whose ego ideal is not t

TABLE I—RESULTS OF TREATMENT IN 94 CASES, ACCORDING TO SEX AND CIVIL STATUS

Civil status	Total	Recovered	Improved	Not improved	Unknown
Male					
Single	15	6	2	5	2
Married	34	21	9	3	1
Separated	18	3	4	4	7
Divorced	3	1	1	—	1
Widowers	—	—	—	—	—
	70	31	16	12	11
Female					
Single	1	—	—	—	1
Married	8	4	2	2	—
Separated	5	—	2	—	3
Divorced	6	2	2	2	—
Widowed	4	2	—	—	2
	24	8	6	4	6
Male and female					
Single	16	6	2	5	3
Married	42	25	11	5	1
Separated	23	3	6	4	10
Divorced	9	3	3	2	1
Widowed	4	2	—	—	2
	94	39	22	16	17

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* Abridged from a paper read before the Society for the Study of Addiction on Jan 18, 1955

drink. After discharge the alcoholic will again meet people who are social drinkers; and to counter balance this influence, the importance of regular attendance at A.A. meetings and of maintaining contact with the hospital—through social workers reunion meetings, the monthly magazine &c —is strongly impressed on our patients.

The Patients

During the last two and a half years 150 alcohol addicts—i.e., alcoholics showing loss of control over their alcohol intake (Jellinek 1952)—were admitted to the hospital as voluntary patients Most of them were admitted because of social difficulties—e.g , continual loss of jobs or marital difficulties All had been heavy drinkers for many years and they were a rather hard core of alcoholics though on the whole not in bad physical shape. The ratio of males to females was 3·4/1 and most of them were in the age group 41–50 The majority of the men were of relatively high intelligence and belonged to the upper occupational groups (I and II) (Registrar General 1951) In several respects our patients are probably not a representative sample of alcoholics in this country

TABLE II—RESULTS OF TREATMENT IN 94 CASES TYPES OF IMPROVEMENT IN 77 CASES WITH KNOWN PRESENT STATE

Sex	Present state unknown	Present state known	Improvement (out of 7 cases) in:				
			Drinking	Work adjustment	Home adjustment	Social adjustment	Subjective feeling
Male	11	59	47	50	13	35	41
Female	6	18	14	8	16	11	11
Total	17	77	61	58	39	46	52

Dry or one relapse

Provisional Results

Alcoholism should not be considered to be ‘successfully arrested’ until abstinence has continued for at least two years (W H O Alcoholism Subcommittee 1951) Most of our patients have not been observed for as long as this. Tables I–IV can be no more than rough guides

77 patients have been observed for periods ranging from six months to two years after discharge from hospital.† Of these 77 39 had had no drink since discharge (‘recovered ’), and 22 had had no more than one relapse (‘improved) (table I) These patients had also improved in other ways (table II) 16 had had more than one relapse since discharge (not improved ’) but most of these were drinking less than formerly and their behaviour and general attitude had improved

In our material four factors seemed to affect prognosis men did better than women (table I) married people better than unmarried (table I), older people better than young (table III) and non psychopathic personalities much better than psychopaths (Henderson and Gillespie 1950) For psychopaths the prognosis is poor (table IV) though there is usually brief improvement The smaller proportion of psychopaths in the older age groups may largely explain the better prognosis of older alcoholics in our material The identification in the mind of the public of alcoholics in general with alcoholic psychopaths is probably largely responsible for many misconceptions

Discussion

Our alcoholic patients have been coöperative easy to handle, and by virtue of intelligence and initiative an asset to the hospital In setting up and running the group we have followed not any preconceived plan but a path of trial and error based on patients reactions to any proposed changes and innovations Despite the lack of planning and experience and the shortage of staff the only major difficulty that has arisen is our inability to admit many alcoholics referred to us

TABLE III—AGE DISTRIBUTION OF RECOVERED AND IMPROVED MALE PATIENTS

Age (yr)	Total	Improved or recovered	Not improved or unknown
21–35	10	4	6
36–50	38	25	13
51–66	22	18	4
Total	70	47	23

Similar schemes based on close collaboration of the mental hospital with A.A and on extensive group therapy, seem to deserve trial elsewhere If alcoholic patients were gathered in a few selected hospitals in each region instead of being admitted haphazardly to any hospital, groups could be formed in the selected hospitals and later in their neighbourhoods These in time would lead to the formation of new A.A branches all over the country and help to teach the public that alcoholism is an illness, lessen the stigma attached to it and encourage patients to seek treatment earlier

Many alcoholics can be helped by outpatient treatment or by A.A. alone but for some admission to a mental hospital may be a beneficial step (Rees and Glatt 1954) It may make clear to the patient how far drink has taken him induce in him a feeling of utter defeat and lead to a personality disruption ' and ego deflation which may be essential for successful treatment (Sargant 1949 Williams 1950 Tiebout 1954) No alcoholic can recover without a sincere desire to give up drinking, and daily contact in hospital with other alcoholics undergoing group therapy may sometimes induce this desire even in patients who entered hospital only to please wife or employer

Community living with other alcoholics rather than the official group psychotherapy sessions seems to be responsible for the change of heart and attitude which relatives often notice after only a few weeks This change of heart seems to begin more rapidly in men than in women perhaps partly because the women are fewer and lack the opportunity of living in a community of alcoholics though they attend the group meetings, which are mixed A mixed unit for alcoholics may therefore be of advantage; the feasibility of mixed units has been proved—e g in our unit for non-alcoholic neurotics (Martin Glatt and Weeks 1954) If patients could be admitted without statutory formalities (as in our neurosis unit) many alcoholics who are afraid of entering a mental hospital because of its stigma might find it easier to do so

TABLE IV—RESULTS IN NON PSYCHOPATHIC AND IN PSYCHOPATHIC MALE PATIENTS

Age (yr)	No of patients	Non psychopaths					Psychopaths				
		Total	Recovered	Improved	Not improved	Not known	Total	Recovered	Improved	Not improved	Not known
21–30	4	1	1	—	—	—	3	—	1	2	—
31–35	6	3	—	1	1	1	3	1	—	1	1
36–40	11	6	1	3	1	1	5	—	2	1	2
41–45	18	15	11	3	1	—	3	—	1	1	1
46–50	9	6	2	1	—	3	3	—	1	1	1
51–60	19	16	12	3	1	—	3	—	—	2	1
61–70	3	3	3	—	—	—	—	—	—	—	—
Total	70	50	30	11	4	5	20	1	5	8	6

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† In the six months since these tables were compiled there have been hardly any changes so the figures hold good for an observation period of one to two and a half years

Summary

A treatment centre for alcoholics at a public mental hospital, working in close collaboration with Alcoholics Anonymous, is described

It is suggested that alcoholic patients should be admitted to a few selected hospitals in each region, where they could form a nucleus for new branches of Alcoholics Anonymous in the neighbourhood

The establishment in mental hospitals of units for alcoholic patients—preferably of both sexes, with admission without statutory formalities—may prove useful for research as well as for treatment

I wish to thank Dr T P Rees, physician superintendent of the hospital, for his encouragement and his advice, the staff for their continual support, our social worker, Miss C Forrest, B A, for her laborious follow-up work, and the London service office of A A. for its keen coöperation

REFERENCES

Bacon, S D (1949) *Quart J Stud Alc* **10** 1
Dent, J Y (1952) *Brit. J Addict* **49**, 33
Glatt M M (1955) *Ibid*, **52** (in the press)
Henderson D, Gillespie, R D (1950) Textbook of Psychiatry London p 388
Jellinek, E M (1951) *Tech Rep World Hlth Org* no 42, pp 20, 21
— (1952) *Ibid* no 48, p 27
Martin D V, Glatt, M M, Weeks, K F (1954) *J ment Sci* **100**, 983
Pullar Strecker, H (1952) *Brit J Addict* **49**, 21
— (1955) *Lancet*, i, 1072
Rees T P, Glatt, M M. (1954) *Ment Hlth, Lond* **14** 11
Registrar-General (1949–54) Statistical Review of England and Wales for successive years from 1948 to 1953 Part I H.M Stationery Office
— (1951) Classification of Occupations, 1950 H.M Stationery Office
Sargant W (1949) *Proc R Soc Med* **42**, 367
Silman L S (1948) *J nerv ment Dis* **107** 127
Tiebout H M (1949) *Quart J Stud Alc* **10**, 48
— (1954) *Ibid*, **15**, 610
W H O Expert Committee on Mental Health (1951) *Tech Rep World Hlth Org* no 42 p 8
— (1952) *Ibid* no 48, p 24
Williams L (1950) *Brit J Addict* **47**, 62

A CENTRE FOR CEREBRAL-PALSIED CHILDREN

CHILDREN are the concern of a great many people—the Ministry of Health, the Ministry of Education, the local authorities, voluntary agencies interested in special aspects of their welfare, and of course their parents, to name only a few To weld all these ministering angels into any kind of family party calls for resource and sagacity In the case of the new Centre for Spastic Children at 61, Cheyne Walk, Chelsea, London, these qualities were evidently at hand, for what has been achieved is a pioneer project, unique of its kind a voluntary centre launched within the National Health Service

It combines a medical centre with a school for children under 5, the school being under the London County Council, and the medical centre under the Chelsea group of hospitals Admiral J H Godfrey, who has been a moving spirit in founding the centre, is also chairman of the hospital management committee of this group, the centre's relations with its parent group are thus of the happiest The National Health Service, in Admiral Godfrey's judgment, has three serious gaps in its provisions for the very young, for the very old, and for pioneer projects In starting a pioneer project for the very young he has had the satisfaction of helping to stop two gaps at once

When the idea was first discussed, two and a half years ago, the South West Metropolitan Regional Hospital Board gave it their blessing—with a proviso that they were not to be asked to make any capital expenditure on it for three years In the event the whole cost—with the exception of the teachers' salaries and the school equipment, which are covered by the London County Council—has been borne by many donors, among whom King Edward's Hospital Fund for London is the chief, the William Johnston Yapp Trust, the London Parochial Charities, and an anonymous donor have also been particularly generous

The centre has its own medical committee consisting of Dr Ian Anderson, honorary director of the centre and consultant pædiatrician to the Westminster and St Stephen's Hospitals, Dr C D S Agassiz, late physician superintendent of Queen Mary's Hospital, Carshalton, Dr Francis Bach, consultant in physical medicine to the Chelsea group, Dr Anthony Feiling, consultant physician to St George's Hospital and the National Hospital for Nervous Diseases, and Dr John Foley, who is the consultant neurologist of the centre Mr Wylie McKissock, neurological surgeon to St George's and the National Hospital for Nervous Diseases, and Sir Harry Platt, president of the Royal College of Surgeons, have joined the committee as coöpted members

Dr Foley holds sessions at the centre at which he diagnoses the children's cases and advises on treatment His room at the centre is close to the records department and library, and next door to the filming room, in which permanent records can be made of the children's progress in walking and coordination The library contains a comprehensive selection of books bearing on cerebral palsy, which have been given by an active league of friends of the centre A file is also kept of all papers published on the subject, and it is hoped that this reference file will in time be so complete that it will be useful to all those working on cerebral palsy who care to consult it

TREATMENT

The centre, which is housed on the ground floor of the Cheyne Hospital for Children, has many comely, well lighted rooms, and these have been decorated with charm and distinction The white entrance hall, with its elegant thin touches of scarlet, lifts the spirits at once Wherever there are stairs a small scarlet handrail runs alongside, set at a level within reach of a small child. The centre takes for the whole day cerebral palsied children who are capable of benefiting by education in the school, and though it has only been open since the middle of April there are already 19 of them attending daily The plan is to add others, one at a time, until there are 24 attending daily, though it may be possible to increase the actual numbers on the strength by arranging for one group to attend on Mondays, Wednesdays, and Fridays and a different group on Tuesdays and Thursdays The number who can usefully attend daily is governed by the number of treatments that can be given the two keen young physiotherapists on the staff find that 12 treatments each are as many as they can complete in a day A few cerebral-palsied children who are not educable are being brought up daily for treatment of their physical condition These, of course, do not attend the school, and indeed they are spoken of as "outpatients" to distinguish them from the school children

The physical treatment room, warm, comfortable, and pleasantly gay, is equipped with two plinths and radiant heat lamps The physiotherapists have recently spent some weeks in Copenhagen studying Danish methods of treatment under Prof Preben Plum at the Rigshospitalet They make good use of ultraviolet light, hot and cold sprays, and massage, including vibration and shaking of the muscles These simple methods, they find, improve the circulation in the blue limbs of these children, and help the muscles to relax

A speech therapist attends twice a week and has her own treatment room where she can give speech training and take records of the children's speech for reference and comparison The tape-recorder in her room has an extension in the corridor outside, so that those interested in a child's progress can listen without interrupting the session They can also watch the child (without themselves being seen) through a darkened glass panel in the door

EQUIPMENT

The well-made furniture of the classrooms and the children's dining room is of a size to suit their age

The centre has the services of a skilled hospital carpenter, a tall upstanding man of 75 who sees no reason for retiring, and who, besides making much of the furniture carries out any adjustments needed to chairs and foot rests, and executes, with beautiful fidelity, any new designs brought to him

The wash basins and water-closets in the children's lavatory are also on an appropriate scale and there is a wooden chair-frame with arms but no seat, which stands over the lavatory pan and enables the child to pull himself up when he rises The wash basins have lever handles to the taps which the children are able to turn on and off more easily than they are the screw type Two competent house mothers look after the needs of the children, prepare them for treatment, and supervise meals

At present there is only one large classroom, its glass doors opening on to a little tiled terrace where classes can be held on sunny days The doors have been specially designed so that they will not shut to of their own accord and perhaps trap fingers An important piece of equipment in the school room is the piano for rhythmic games are useful in helping to establish control of muscles Outside, in a pretty little garden a new classroom is going up, modern in design with windows all along one side The garden overlooks another garden—that of Chelsea Old Church, now rising again from its wartime ruins and the keen gardeners among the congregation, who keep the church grounds in flower, are also going to lend a hand with the centre's garden At the bottom of the building is a yard with a perambulator garage but some ideas are already stirring about the centre's own van—or perhaps two vans—to be driven by volunteers who would go round collecting the children in the morning and delivering them back at their own doors in the afternoon

The most striking thing about this centre is its happy atmosphere The affectionate kindness with which these intelligent handicapped children are treated and taught is a final expression of the whole spirit of the place

REGIONAL HOSPITAL BOARDS AND BOARDS OF GOVERNORS OF TEACHING HOSPITALS

THE Minister of Health has reappointed the following as chairmen of boards

Newcastle Regional Hospital Board —Edward F Collingwood, C.B.E., D.S.C J.P

United Manchester Hospitals —N M Agnew

Bethlem Royal and Maudsley Hospitals —Mrs. F C Ormerod.

Hospital for Diseases of the Chest —Widdrington Stafford.

Queen Charlotte's and Chelsea Hospitals —A J Espley C.B.E., J.P

The Hospital for Sick Children —Claude A. Lucas T.D M.A LL.A.

Eastman Dental Hospital —A. D Page

MEMBERS OF BOARDS OF GOVERNORS

The following doctors have been appointed to boards They will hold office till March 31 1958 New appointments are indicated with an asterisk.

St Bartholomew's Hospital —F C W Capps, Sir James Paterson Ross.

London Hospital —H. B May J Stanley Thomas Vernon Thompson, Eustace Hoare Clifford Wilson.

Royal Free Hospital —Geraldine Barry G E Breen D H. Geffen, J C R Hindenach * J S F Pollitzer

University College Hospital —Cecil Flemming, J D S Flew K L. Harris S Cochrane Shanks.

Middlesex Hospital —* W R Winterton.

Charing Cross Hospital —Norman Lake, * A Doyne Bell * Lionel Taylor

St. George's Hospital.—Sir Claude Frankau, Hugh Gainsborough, Alastair Hunter D Stark Murray * H H D Sutherland (till March 31 1956)

Westminster Hospital —F D Hart

St Mary's Hospital —Joel Green, * J W Litchfield * F W M. Pratt

Guy's Hospital —E. R Boland, A. Talbot Rogers, E G Slesinger * A. H. Douthwaite * Grant Massie

King's College Hospital.—F S Cooksey, Sir William Gilliatt, V F Hall, J H. Peel.

St Thomas's Hospital —W G Barnard, J Forest Smith, C H Vernon, R H O B Robinson, * R W Nevin.

Hammersmith West London and St Mark's Hospitals —John McMichael Charles Newman, Maurice Shaw

The Hospital for Sick Children —A P Norman Wilfrid Sheldon

National Hospitals for Nervous Diseases —Sir Francis Walshe * Redvers Ironside * Alan Kekwick.

Royal National Throat, Nose and Ear Hospital.—Adam Gray C Gill Carey * J W Cope

Moorfields Westminster and Central Eye Hospital —R. C. Davenport, Sir Stewart Duke Elder * Cyril Shapland.

Bethlem Royal and Maudsley Hospitals —Sir Allen Daley D L. Davies, A. Harris, Doris Odlum, F R Winton

St John's Hospital for Diseases of the Skin —R M. B MacKenna, J E M Wigley

Hospitals for Diseases of the Chest —Sir Clement Price Thomas, J G Scadding J Smart * Sir Geoffrey Todd.

Royal National Orthopaedic Hospital —H Jackson Burrows John Cholmeley

National Heart Hospital —Graham Hayward G H Jennings P H. Wood

St Peter's St Paul's and St Philip's Hospitals —Clifford Morson J G Sandrey

Royal Marsden Hospital —Sir Stanford Cade D W Smithers, Alexander Haddow (till March 31 1957) * W A Mill.

Queen Charlotte's and Chelsea Hospitals —S G Clayton, Charles Read * Humphrey Arthure (till March 31 1957)

Eastman Dental Hospital —Frank Wilkinson * R R Stephens

BIRTHDAY HONOURS

THE *list appearing in our last issue omitted the names* of two members of our profession on whom honours have been conferred They are:

O B E (Military)

Wing Commander LILIAN GERTRUDE MOORE M B Belf., M.R.C P.E R.A.F

Wing Commander JAMES CLARKE TAYLOR, M.B Glasg R.A.F

NEW MATERNITY HOSPITAL IN CARDIFF

THE steel skeleton of a new maternity hospital stood beside the Cardiff Royal Infirmary throughout the war years. On the outbreak of war in 1939 building was discontinued and it was not until May of this year that the hospital admitted its first patients. The hospital, which is administered by the board of governors of the United Cardiff Hospitals, has its *own matron and is a part-I training-school for midwives.*

Of the six floors the top two are devoted to nurses quarters but they have been so designed that they could readily be converted to take patients. On the ground floor are antenatal and baby clinics, X ray department lecture-theatre demonstration room library kitchens, administrative offices and the clinical research laboratories of the department of obstetrics of the Welsh National School of Medicine The patients are accommodated on the remaining three floors. Each floor has 27 beds and, apart from minor variations in the nursery arrangements, they form identical units consisting of delivery suite of two first-stage rooms and two delivery rooms nurseries, five 4 bed bays, and seven single rooms. On one of the floors is a premature baby unit, and on the same floor one of the delivery rooms is equipped as an operating theatre

The babies will ordinarily be nursed with their mothers, but there is enough nursery space to accommodate all the babies at night. Continuity of nursing care for the mother will be ensured by having the same staff in charge of antenatal beds delivery room, lying in beds, and nursery for normal babies Anæsthetic gases are piped to the delivery rooms and oxygen and suction points are provided in the wards. Sterile water is laid on and elaborate antistatic precautions have been taken in constructing rooms in which anæsthetics may be given

The new hospital is to be officially opened on July 12 by the Duchess of Kent.

The Widdicombe File

XXVI THE HOUR OF THE ANGEL

Dear Charles,

I'm exceedingly glad to hear you can take our rooms at Mrs. Woof's in August. Rooms on the Devon coast in August at six guineas a head are not to be sneezed at ever, and hers are worth double. She will look after you and the family admirably. Wychecombe Bay itself is overrun now by caravan camps (the hills around have been terraced for caravans till they look like the work of Ancient Britons in Somerset), but Wattecove a mile away is just as good, and deserted because it has no motor road.

Let me tell you though before you go, as an awful warning, of a thing which happened last year. Did you ever have to resuscitate the Apparently Drowned? I did, and it was not a pleasant experience.

It was, you remember, an August of lousy weather last year, and the day in question, though rainless and almost warm, boasted about five eighths of an onshore gale. Beatrice and I, very much *en famille*, came over the cliff path into Wychecombe Bay towards lunch-time, intending to buy apples at the caravan camp shop. As we came in sight of the beach we could see two most ominous looking huddles of people at the water's edge. There was a man leaning over the end of a stone wall, watching them through field glasses. “ No, it's nothing,” he said. “ Rowing boat brought something ashore—fish, I expect.” Reassured, we yet urged our litter a little faster downhill. Halfway down, five wasted minutes later, I began to doubt the diagnosis of the fool with the field glasses, and soon was running as hard as I could across the wide wet sands. The two huddles meant two bodies, and they had been pulled out of the sea just before we caught sight of the beach.

There were a lot of people on the beach, and I had some difficulty in getting to the centre of the first knot. There lay there a heavily built, thick-necked man of 40 odd. He lay on his face on the wet sand, with two towels and a raincoat over him but nothing under him. One of the rescuers was applying artificial respiration (Schafer's method, more or less) at about 60 to the minute. Seven others at least were rubbing his limbs violently. No one was paying any attention to his airway. Two stout gentlemen were contesting who could shout “ stand back, give him air ” most importantly, though the close ring of onlookers was in fact our only shelter against the wind. There were all the makings of farce, except the happy ending.

He was pale and cold and bluish round the ears, but looked, to my inexpert eye, extremely alive. I said, loud as I could, “ I'm a doctor. Who's in charge here?” The assembled company looked at each other, but admitted no leader. They looked then at me, and found in my ancient ski jacket, torn shorts, bare legs, broken sandshoes, and peeling nose little to reassure them. This, they thought, could hardly be a *proper* doctor. The feet nearest the patient's head were reluctantly moved away enough to allow me to kneel down by him. I felt a doubtful carotid pulse, manœuvred the head into a position rather more compatible with a free airway, and attempted to take stock. You must remember at this point that I had never dealt with drowning before, that my last clinical responsibilities had ended shortly after V.J.-day, that this case came out of the blue of a holiday which was family ridden and rain soaked but otherwise completely placid, and that I had only the moments of my run across the beach to recondition me to this most unfamiliar emergency. There were two problems: what to do, and how to get someone to do it while I went to look at the other body.

At this moment a heave in the crowd brought up a blank faced young woman, with a chorus of “ She's a nurse, doctor.” She remained dumb, but took over the head with some appearance of knowing what she was doing. I exhorted the artificial respirator to slow down his rate, and told the nurse to keep him at it, and escaped, thankfully I'm afraid, to survey my second problem.

At the centre of the second huddle, in most respects just like the first, was a boy of 13 or so. His nose was nearly buried in the sand, and vigorous artificial respiration was being applied. All appearances to the contrary however, his airway was clear, and indeed as I turned his head the air could be heard bubbling quietly in the larynx with each heave of the resuscitator's body. The resuscitator was himself panting with his efforts, and I suggested he slowed down a little. This was received with no favour: clearly he considered that the harder he worked, the more good he must be doing. But I persuaded him to stop a moment while we got some towels under the body, and in that moment the body had the wit to produce a faint gasp of spontaneous respiration. We waited, breathless ourselves, for half a lifetime—thirty seconds I suppose—and it was repeated. Here at least was one success.

Obviously what he needed was assistance to deepen each spontaneous breath, and the two of us worked at the timing of it for a minute or two. It looked better and better. One would have supposed that our exhilaration would have equally possessed the onlookers. But no, survival was an anticlimax, and the circle was thinning. The wind whipped in again, and I wasted another minute or two in expostulation before anyone would hurry up the beach to speed the stretcher which it was vaguely assumed that someone was fetching. The huddle of bowed heads round the other body showed there was no such success yet in that quarter.

I elbowed my way back into the centre. The nurse had vanished—how or why I never discovered (she cannot, I think, have been a real nurse—perhaps a nurse maid misidentified and too overwhelmed to disclaim it). There was a veiledly acrimonious dispute going on over the resuscitation roster (“ Old man, you've had enough now, you're tired ”) and the rate was still around 60. The body looked much the same, but by contrast with the one I had just left looked much more dead than it had before. I could not feel the carotids. The resuscitators proved incorrigible in their adherence to an excessively rapid rate, and I decided (reluctantly, for it lost me my freedom of movement) to resolve their arguments by taking over myself. The body was cold and wet as I straddled it, and the fat muscular chest ominously stiff as I leaned forward on it with straight arms and ostentatious slowness. I had time at least, for the first time since reaching the beach, to begin to wonder where we went from here. The ring of staring faces remained as blankly unhelpful as the casual urban audience of a hole in the road. The tide began to lap round their ankles: we would soon, willy-nilly, have to move.

Blessedly at this point the matter was taken out of my hands. Simultaneously there arrived the local G.P., a St. John's man, and the police. The police (sixteen stones of him) brought a van and a stretcher, the St. John's man experience of these affairs beyond mine, and the G.P. not only knowledge and experience but the dress, bearing, and bag of a real doctor.

After that all went as it should in the books, and there's not much point in continuing. The boy was soon mended, the man proved to be beyond recall. Harry Hawke did the ys for the coroner and the coroner told us how unwise is to bathe in even the safest of West Country bays when the tide is low and the wind high And that was that Perhaps the three prosperous little caravan camps who live on the bay have provided a stretcher between them this year and got one of their staff trained in resuscitation or perhaps they've forgotten It might be an idea if you inquired—tactfully

For myself I am still more than a little harrowed by the memory Probably what I thought was a carotid pulse when I first saw the man was an illusion—my own rapid pulse from running even a transmitted pulse from the persistent massage school on the legs But I will never be certain, and never be quite certain that we could not have saved him

That damned ignorant staring helpless crowd still haunts me

> I know not whether I am proud
> But this I know I hate that crowd.

Not one man or woman in that sample of 200 or so of the prosperous lower middle classes of England knew a thing about first aid for the drowning beyond the barest notions of Schafer's method No one had any notion of organising the crowd and assuming some sort of responsibility One wartime sergeant of gunners remembering something of his authority, and a few fuglemen to give a lead in *following him would have made all the difference*. By the time I arrived on the scene the mob was lost disheartened convinced of its own futility and the futility of any further effort, passively panic-stricken

Not that I'm very happy about my own part in the affair I did most of the right things (barring the Holger Nielsen which I didn't know at all) but I had to work them out from first principles and wasted time and thought getting started on them I neither looked like a doctor *nor* acted with the instantaneous decision expected of one and lost the moment of confidence in which I might have imposed myself on the mob as the needed boss.

You and I, Charles have retired so far as our jobs are concerned from the life and death responsibilities of clinical medicine into our laboratories We may have major decisions to make but we make them quietly in our own place and almost in our own time We do not have to make them with a thumb on the artery in the theatre or blanching under the stench of vomit in a crowded basement bedroom We keep our side of the bargain we work under laboratory conditions, and we accept the responsibility for producing results of a laboratory standard of accuracy But outside our working hours at the roadside or on holiday by hill or river or sea the accident catches us unawares, without our defensive armour of forms and bottles and reports housemen and secretaries and technicians and we are plain doctors again, with a life nakedly in our hands to save or lose. It is Ithuriel's hour—

> the test
> Of our sole unbacked competence and power
> Up to the limits of our years and dower
> Of judgment—or beyond.

I don't seem to have come out of my hour with the angel more than middling It boils down to this though the gift of confident authority comes of knowing what to do. There are occasions when even the illusion of knowledge is better than nothing at all I know that if ever again I encounter a similar situation I will blow out my chest screw up my courage tick off the biggest man in sight at once and act not merely the good doctor but people's idea of how a good doctor should act But it's much easier if one knows what one's up to

Do you know as much first aid as a moderately good St John's man Charles? Disgracefully few pathologists do Come to think of it 50% of the profession are probably just as bad We like to be called "Doctor" we accept our little perks like the occasional chemist's discount no jury duty, and side wards in hospital for us and our families we do not even question the G M C's view *that the man who qualifies must already be capable* of the basic responsibilities of a doctor But emergency not so rarely shows us barely worthy of our honourable title

You'll enjoy Mrs Woof's Charles But read up a few first aid manuals before you go and make sure you know the Holger Neilsen I need hardly say I have

Yours
PETER DAVEY

PS —I've just seen an excellent little book from New Zealand called *Artificial Respiration* by T O Garland (Faber & Faber 6s 6*d*)—the best I know of so far

Public Health

Uses of Radioactive Waste

WORK on radioactive waste in the United States and at Harwell suggests that many medical and industrial uses can be found for it, and a new research group has been established at Harwell to investigate the possibilities.[1]

One line of research will deal with the preservation of food by exposing it to irradiation from waste. It is possible that the widespread use of radiation sterilisation may reduce, or perhaps even abolish, the need for refrigeration to keep food fresh For example, the Royal Navy is already being supplied from Harwell with potatoes that have been treated so that they will not sprout In America it has been found that when meat is irradiated so that it keeps indefinitely it has a different taste—though the taste is normal if the meat is only partly treated to preserve it for shorter periods. Full scale experiments will begin at Harwell this year and it is hoped to solve the problem of taste within two years. Dr H Seligman, head of the isotopes division at Harwell has said that the main concentration of British food experiments may consist of attempts to improve the "shelf life" of food rather than to preserve it indefinitely, tomatoes, for example, can be made to last fifteen days on a shelf before going squashy rather than five days as now It will also be possible to treat food before it is packed

Radiation from waste can also be used to speed up chemical processes, such as the preparation of gammexane; and there are many possibilities in the manufacture of expensive drugs such as hormones The sterilisation of pharmaceuticals is another application and this will be particularly valuable where heat cannot be used as with penicillin and streptomycin As for radiotherapy the most successful fission product seems to be cæsium 137 and radiation from large sources of *cæsium may turn out to be the most satisfactory method* of radiotherapy so far evolved

In industrial processes, it has been found that irradiation makes 'Polythene' more resistant to heat so that cables can be used at higher ratings and temperatures. Vulcanising processes can be speeded up and the application of irradiation in oil refining is being further investigated.

Poliomyelitis in Barnsley

There have been 22 confirmed cases of poliomyelitis in the Barnsley area of Yorkshire The medical officer of Health Dr G A W Neill has said that the outbreak is not a serious one,[2] but the usual administrative precautions have been taken including the stopping in schools of pursuits likely to cause physical fatigue

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1 *Times* June 15 1955
2. *Manchester Guardian* June 20 1955

Parliament

Future of the Social Services

THE fourth day of the debate on the Address (June 14) was reserved for a discussion of the social services Dr **EDITH SUMMERSKILL** opened the debate by regretting that the Queen's Speech contained not one word on the sick and the aged She went on to ask the Minister of Health how many new beds would be provided this year for our mental hospitals, how he proposed to recruit extra staff for these hospitals and the sanatoriums, and to provide, through the local authorities, home helps and halfway homes for old people

She also regretted that the recommendations of the Gowers report were apparently to be so tardily implemented The Gracious Speech announced that a Bill was to be introduced on the health, welfare, and safety of those employed in agriculture and forestry, but no mention was made of workers in shops and offices and on the railways Turning to the services under the Ministry of Pensions, Dr Summerskill declared that the pigeon-holing of the Phillips report was not only discourteous to a distinguished committee but showed a callous disregard for the needs of the aged She also asked whether the proposed extension of family allowances would include children at all colleges, and also mentally retarded children who remained dependent on their parents

Mr **OSBERT PEAKE** Minister of Pensions and National Insurance, defended the priority given to the Bill for the protection of workers in agriculture and forestry on the grounds that these industries were becoming ever more mechanised and the accident-rates had risen If there were time a Bill dealing with safety and health on the railways would also be presented The Bill dealing with shops and offices would be much the biggest Almost certainly it would be impossible to introduce it in the first session The Government had in mind that the age-limit for family allowances should be 18 After all, the scheme was in respect of children, and to go on counting people as children after they had qualified for National Service would seem to be going rather far Some provision would be made for handicapped children

As a result of the changes recently made in the pensions scales of benefit, he continued, about 111,000 fewer people were drawing assistance today than 2½ years ago There was every sign that we could look forward to a steady reduction, and he believed that we might approach the Beveridge idea of a society in which the means test was hardly ever exercised Much had already been done to rebuild our social services The value of pensions and benefits, which 3½ years ago had steadily fallen was now fully restored and provided better purchasing power than ever before There was still much to do In the first session of this new Parliament the main emphasis would be on education and housing, but the Government believed that, given freedom from industrial disputes, given a reasonably steady cost of living and increased productivity, the beneficiaries of the social services could look forward to a better future

Miss **EDITH PITT** thought that we were getting good value for the £463 million we spent on the health service, but she believed that we could get even better value if we concentrated on preventive work She would like to see more emphasis on the use of the family doctor Since the 1953 award he was better paid, but he still had too little time to pay full attention to every member of the family Sir **FREDERICK MESSER** was troubled because we seemed to be separating health from welfare, and this in his view was a big mistake The lack of integration was particularly marked in the welfare of the aged

Mr **J K VAUGHAN-MORGAN** saw an increase in domiciliary services as a first line of defence in health, and he hoped that the reform of local government forecast in the Gracious Speech would include some means of closer association between the local authorities and the health services He recalled that when the Ministry of Health was founded in 1919 it was given the positive duty of "promoting the health of the people" Since then its powers had been whittled away until its main preoccupation was curing ill health rather than preventing it Many of its duties had been reshuffled to the Ministry of Local Government and Housing He would like to see the industrial health services transferred to the Ministry of Health The expected report of the Guillebaud Committee and the promised reform of local government would, in his view, give us a chance to rebuild the National Health Service on a sounder basis

PAYING FOR SECURITY

Miss **ELAINE BURTON** suggested that in this century we had established the principle that the community must provide social services for its citizens In the years to come she hoped that we would develop the services with the aim that they should be given to a citizen as a right, without test of means To achieve this money could be provided in three ways by graduated contributions, by a social security tax, or out of general taxation In her view it was wrong in this modern age that social services should be paid for by all citizens at the same rate, irrespective of what they earn

Mr **DOUGLAS HOUGHTON** also examined the basic aims of social security today Are we prepared, he asked, any longer to think of Beveridge minimum subsistence pensions? Were we not to think now in bolder terms of the construction of a cost-of-living index for old people The standard pension for married couples was now only a third of the average wage That was not adequate social provision for retirement We must, he suggested, look at our scheme of social security more as a national superannuation scheme than as an insurance scheme

Mr **JAMES GRIFFITHS** described the flat-rate contribution as "the most aggressive tax we have" The only person who now paid the full insurance contribution was the one who did not earn enough to pay income-tax Unless a fundamental change was made in our system of social insurance, National Assistance would become increasingly, not a residual service, but an integral part of our welfare system

THE MINISTER'S REPLY

Mr **IAIN MACLEOD**, the Minister of Health, pointed out that the Queen's Speech covered only one aspect of the programme which the Government had outlined in their policy statement Of the subjects affecting his Ministry the only promise of legislation was for medical auxiliaries He did not think it was likely that that legislation would be ready for this session, although considerable progress had been made

Schemes already approved and in current building programmes for England and Wales would provide 7000 new mental-deficiency beds and there were under consideration schemes which would provide at least another 2000 1000 extra beds had been provided in mental hospitals since 1948 Beyond that, 3000 had been approved in the current programme and proposals for another 500 were being considered The staff deficiency on the mental side might be estimated at about 10,000, though the nursing staff as a whole had been slightly increasing year by year The home-help service had gone up from 11 000 at the end of 1948 to over 33,000 at the end of 1954 In the last year 62% of the cases looked after by home helps were classified as chronic sick There was no absolute duty under the National Health Service Acts to provide this service, but all local authorities provided it Some time this year—probably in the autumn—the Government would receive a report from the Guillebaud Committee The review and any reconstruction in the National Health Service that would follow would be carried out by the present Government

The social services ought now to be breaking clear of their teething troubles It should be possible to find some principles which should guide them in the period ahead First, he thought that increasingly responsibility should go where the work was done That would mean of course a trend in responsibility downwards, and this was one of the matters which were being considered by the Ministers concerned with local government Secondly, he thought they should try to bind together more closely in comradeship the voluntary and the State services.

They should try to get leagues of friends increasingly active in the hospitals, and the hospitals should be more open than they were now People should begin to feel that they owned the hospitals The third and last principle was that they should try to encourage diversity in the social services. In the health service people should not be prevented from buying privacy for themselves or their families when they were ill. He did not believe that any single pattern could cover the range of the social services and it was therefore of great importance that they should encourage independence in every possible way Finally it had to be remembered that the social services had to be earned and paid for by the prosperity of the country they were not a gift of Government.

QUESTION TIME

Poliomyelitis Research in Scotland

Replying to a question Mr James Stuart secretary of State for Scotland, said that the Scottish Hospital Endowments Research Trust had accepted the first application for financial assistance for research into poliomyelitis and other virus diseases. This consisted of a grant of £3000 to meet the cost of equipment which would be required shortly in the new virus laboratory at Ruchill Hospital, Glasgow

Crash Helmets

Mr Barnett Janner asked the Chancellor of the Exchequer whether he would consider taking steps to remove purchase tax from crash helmets, in view of the recent recommendation of the British Medical Association and the fact that some [illegible] million a year is involved in treating people in hospitals who are unable to afford to buy this article —Mr R A Butler replied This is a matter which I have considered very carefully in view of the representations made to me but I am not yet convinced that motor cyclists are deterred from using these articles by the few shillings tax involved Mr. Janner Is not the Minister aware that some 1300 deaths a year are caused by these helmets not being worn ? Even if the persons themselves are not prepared to purchase the helmets, does he not think it the duty of the State to afford facilities for those helmets to be used ?—Mr Butler : I hope that people will wear these helmets but I am not at present in a position to remove the tax

Sir Frank Medlicott : Will the Minister bear in mind that purchase tax was originally imposed partly to discourage people from buying things ? Is it not time that we removed this particular discouragement from this very valuable and life-saving article ?—Mr Butler There are other forms of important protective clothing which are still taxed, and I am afraid that I cannot go further in my answer today

Myxomatosis

Replying to a question, Mr Heathcoat Amory Minister of Agriculture said that his department had examined surviving rabbits from many parts of the country and of these 39—or about 10%—were found to have acquired immunity to myxomatosis. It was not however possible to say whether this proportion was representative for the country as a whole Mr Somerville Hastings Is there any evidence that this immunity is carried to the next generation ?—Mr Amory : I understand not, except possibly for the first few weeks of a young rabbit s life

Heroin Addiction

Replying to a question Major Gwilym Lloyd George Home Secretary said 52 heroin addicts are known in England and Wales and 2 in Scotland. At the present time there are no persons in respect of whom addiction is suspected but not proved Drug addiction is not compulsorily notifiable in this country but I have no ground for thinking that there is any substantial hidden addiction From Jan. 1 1950 to date 23 persons were convicted in respect of 24 offences involving heroin, one person having been convicted twice Of these 23 persons, 15 are known heroin addicts and 1 person who has since left the country was suspected to be addicted to the drug

Prices of Drugs

Replying to a question, Mr Iain Macleod said that since May 1953 of the 73 most expensive and frequently prescribed proprietary preparations, 29 had been reduced in price (many between 20% and 60%) some of these reductions reflecting in part reductions in the basic drug prices. In addition special provisional reductions ranging up to 20% were recently arranged with manufacturers in the prices of 19 proprietary preparations During the same period the prices of certain important basic drugs and their corresponding products had been reduced some of them several times. These voluntary reductions included some recent ones (since June 1954) ranging up to 20% in the prices of penicillin streptomycin chloramphenicol and hormone and vitamin products

Poliomyelitis Vaccine

Replying to a question, Mr Macleod said that a member of the staff of the Medical Research Council had just returned from a visit to the United States where he had been studying the latest developments regarding anti poliomyelitis vaccine No explanation for the Cutter vaccine incident had yet been found but it was possible that certain batches contained live virus He understood that the safety tests to be applied to the vaccine in the United States had been greatly multiplied, including a closer control of manufacturing processes. Pending the introduction and application of similar measures here, the Medical Research Council had postponed the start of any field trials This would probably involve a postponement until the late autumn of this year

A Doctor and the Rail Strike

Mr James Baird asked *the Minister of Health* what position under the National Health Service was held by the doctor who declined to see one of his patients, the wife of a railway striker until the strike was over —Mr Macleod replied that the doctor was a part-time consultant to the board of governors of the United Birmingham Hospitals and to the Birmingham Regional Hospital Board

Mr Baird : Was the doctor s action not completely unethical and did it not amount to political discrimination ? Will the Minister see either that the doctor changes his principles, or that his name is withdrawn from the National Health Services list ?—Mr Macleod : If there were any question of breach of contract within the National Health Service it would be a matter for which I would be glad to answer but if it is a question of medical etiquette which the hon member seems to raise that is not for me nor is the matter of a private arrangement which a doctor might make with his private patient Mr Baird : Is it not a fact that this doctor says that his principles do not allow him to see these people ? Surely his principles must operate in the National Health Service as a whole and what he is saying is that he will never see a patient on strike ?—Mr Macleod Equally there is a matter of principle involved in my reply I cannot reply on matters for which there is no Ministerial responsibility at all, and that I am afraid, is the case in this regard

Criminal Offences by Mental Defectives

Mr Kenneth Robinson asked the Minister of Health why under circular H.M (55)46 he required the police to be informed of sexual acts by certified mental defectives, in addition to the normal report to the Board of Control whether he was aware that medical superintendents had been informed by his department that such reports to the police were still discretionary ; and if he would revert to the earlier procedure by withdrawing the circular —Mr Macleod replied : The circular was issued after consultation with the Home Secretary because the earlier procedure which had only been in force since 1951 did not have sufficient regard to the duty of the police to investigate criminal offences. The circular advises but does not require cases to be reported to the police I am aware of no good reasons for its withdrawal

Mr Robinson Surely the Minister is not suggesting that the police should prosecute in cases like this ? Is it not a fact that the old arrangements have been working quite satisfactorily ? Why does the Minister want to place this additional burden on medical superintendents ?—Mr Macleod There are certain cases which by the 1913 Act are in effect criminal offences which come within the terms of the circular We are getting back to the practice which operated before 1951 This is a matter of doctor patient relationship and the final decision of whether the police should be notified is left to the medical superintendent

In England Now

A Running Commentary by Peripatetic Correspondents

FOR the past five weeks I have been lying in bed healing a duodenal ulcer. For most of the time I have been in my bed at home looking out on what is to me one of the pleasantest views in England. The foreground is a field, with cows in it, sloping gently to the village a quarter of a mile away. The village is—just an English village. It is not one of the show places, and no circular tours call there; but it has a nice old church, just in the right place, and houses of every period living happily together. There is a little river at the foot of the hill and the backcloth is a low range of tree covered hills. It all looks as though it had been there a very long time.

While I have been in bed the scene has shed its winter mantle and put on its early summer one. At first the trees were bare and at the end they were clothed in the lush green of summer in the West Country.

Then I developed a small complication and the friend who was looking after me decided that I must go into hospital for a short course of treatment; nothing drastic but something with plenty of needles in it.

The hospital has a long and honourable tradition, and like our village it has just growed over the years. My guest room is tucked away in a small building in the back yard of the main one—called, rather inappropriately, the "Cottage"—and the rest of the back yard is filled with a hotchpotch of buildings of every shape and size which epitomise the history of medicine in the last two hundred years or so. I am afraid that, unlike our village, they are not beautiful. The "Cottage" is one of the early ones and was built as an isolation block at a time when it must have been badly needed. Its internal decoration is Doulton unadorned, with glazed white tiles from floor to ceiling, and it must have been the pride and joy of some long dead apostle of hygiene. However, between me and the hideous back of the "new" X-ray department there is a garden. It is none of your sooty urban flower beds, but a real garden, with a real tree, in which the birds sing just as sweetly as they do in my garden at home. When I admired it Sister said "Oh, but you should have seen it last week when the tulips were at their best." Sooner or later I expect the cottage will be pulled down to make room for the new department for cosmic ray treatment or some such. I hope that the "cottage" garden will not have to go too.

* * *

I cannot honestly say that I appreciate the modern composers or the twelve-tone system which the pundits talk about. However, I confess that I was rather put out by the cat the other day. She was sitting quietly washing herself when suddenly she perked up at the sound of Hindemith. She strolled over to the radio, quite casually, and sat down to listen until the end of the concert piece and then returned to her basket and her toilet. It is disconcerting to be outclassed by one's own cat. I now blush at my staple diet of Mozart and Beethoven.

Have you ever noticed how little difference there is between babies and small animals? My cat's love of Hindemith reminds me of a friend's experience lately. He and his wife had moved temporarily into a hotel, taking with them nothing but the bare essentials and, of course, the baby. The child, aged eighteen months, was completely frustrated all day and most of the night. It defied three grains of chloral. It became semi-comatosed on five grains only to awaken two hours later as noisy and as troublesome as ever. And all because it missed its music. It was happy only while stamping around the floor or beating the side of the cot with a metal spoon in time with the music. My friend had to bring the family radiogram to the hotel. The latest report from the distracted father was that anyway it showed a growing appreciation of Bach.

Now this you will realise was no mean feat. In a matter of months this child had completed what the experts aptly call "the musical pilgrimage" which (they say) starts with Chopin and Liszt and ends with Bach. Surely in this day and age with Three Blind Mice, Little Bo-peep, later with Men of Harlech, later still with the Lord High Executioner, we are handing out inferior stuff for the all-impressionable, all-embracing minds of our offspring. The time has come when Listen with Mater should be Listen to Mahler. By five years of age our children will surely be ready to benefit by The Exposition of the Fugue for Five-year Olds, the Contrapuntal Element in the Classics for Children, or even Tchaikovsky for Toddlers.

* * *

What Samuel Pepys called his "House of Office"—which was a source of offence between him and his neighbours—was in my boyhood called a "W.C." The term indicated the change in domestic life wrought by the introduction of an abundant piped water supply and the disappearance of the well. A water, as opposed to an earth, closet was something of a novelty—such as "H and C" is occasionally today. Victorian England refined the water-closet into the "W.C.," though in rather unsophisticated circles—as it seemed to me, across this span of time—the rather *démodé* word "closet" was sometimes used alone. In family circles the "W.C." was apt to be abbreviated to the "W." The insidious ingression of Americanisms (is it not indelicate to talk of the breast of a chicken; and does not your hostess ask you if you prefer a "limb" or "the chest"?—unless maybe the deep-frozen animal is now purveyed in "portions") ousted the "W.C.," abetted in this by material progress, and gave us the "lavatory" which today has become the "toilet." International air-travel has guilded this sophistication and air hostesses tell us that "the ladies' powder room is at the back of the plane on the right hand side" (meaning on the starboard side aft). Our Georgian ancestors, or some of them, had "powder closets," and it is a nice speculation whether the "powder room" will revert to the old form, and full circle bring us back to the "closet." But terminology advances along strange paths, so that in a recent visit to the Western Hemisphere all I could find offered for man's, or woman's, need were "rest rooms." I didn't want to rest and, finding no alternative label, vaguely wondered if in some obscure annexe of that doubtless commodious apartment there might be the facilities required. I entered, and found merely a W.C.! *Plus ça change* . . .

* * *

She was a motherly old body, but her symptoms seemed to be functional, so the psychiatrist's aid was sought. He interviewed her in the ward side-room, and some time later the sister asked her how she had got on. She had apparently enjoyed her chat, had thought the doctor was a nice young man, but was sorry to find him so restless, and smoking so many cigarettes one after the other. She really felt it would do him good to see one of these psychiatrists about whom she had heard so much.

* * *

A new typist and a nodding consultant informed me in the discharge letter that old Mrs. Claypole "had lived for several months on bread and butter and Global Salts." The new treatment for *Weltschmerz*, no doubt?

* * *

CHILD GUIDANCE

Be strict in teaching cleanly habits but to see
Evolving an obsessional personality;
Be lax and you may live to curse
Enuresis or worse.

Chastising for each misdemeanour surely bends
The character in sadomasochistic trends;
Never punish and impress
A selfish lawlessness.

Exhibit deep concern and dote unceasingly
To make the child fixated in a high degree;
Deny all love and note oft times
Delinquencies and crimes.

Perhaps the very ancient Chinese wisdom lends
Some help to our debating analytic friends:
Always avoid extremist zest,
The golden mean is best.

Letters to the Editor

QUARANTINE MEASURES IN POLIOMYELITIS

SIR,—Might I be allowed to congratulate the medical officer of health and the general practitioners concerned on the results of their quarantine measures in the outbreak of acute poliomyelitis reported in the article by Dr Goffe and Miss Parfitt in your issue of June 4 Only one further case developed, and the summer outbreak, which we have learnt to fear following the occurrence of later cases in an area, did not occur

I should also like to congratulate Dr Goffe and Miss Parfitt on their confirmation of the high incidence of infection in the contacts of the 4 cases of acute poliomyelitis (8 out of 17 household contacts, and 1 child in the village school attended by 3 of the contacts, were excreting the same type of poliomyelitis virus in their stools) It is on this concentration of virus round the index case that the justification for the inconvenience of quarantine of contacts depends

While welcoming the findings of these laboratory workers however one must question their interpretation of them So far from being satisfied with the success of the quarantine measures, they write Quarantine measures applied in this community did not prevent the spread of infection ' and 'infection was widely disseminated in the community ' Since the disease failed to spread and *no attempt* was made to study individuals who were not either direct or indirect contacts it is difficult to see on what they base these conclusions surely not on the finding on two occasions (January and March) out of four (February and May) of virus of the same type (type I) in town sewage draining other houses than the cases ? The relation between virus in sewage and acute poliomyelitis above ground is at best a very loose one—indeed as they point out, type II virus had been isolated from the same sewage on two occasions in the previous year without accompanying disease above ground—and such findings can hardly be regarded as convincing evidence of widespread dissemination

What really appears to have worried these workers was that their infected contacts continued to excrete virus in their fæces beyond the recommended period of quarantine. 'Quarantine they write, 'seems to be of doubtful value *in practice* if at the end of three weeks three-quarters of the infected members are to be returned to the community still carrying virus ' (my italics) They mean of course, that its value is doubtful *in theory* or more accurately, *in their theory* *In practice* it is of value, and there is a perfectly good theory to explain this—namely that infectivity and fæcal infection ' are not synonymous It is after all only against infectivity that quarantine restrictions are aimed and there is ample epidemiological evidence that, at any rate in countries with adequate disposal of sewage the period of infectivity corresponds not with the known prolonged period of fæcal carriage of the virus (three months is the figure given by the expert committee of the World Health Organisation which Dr Goffe and Miss Parfitt quote) but with the very much shorter period of pharyngeal carriage

Had these workers studied virus in the pharynx instead of virus in the fæces they would have understood why in both practice and theory quarantine need be enforced only for three weeks following contact as recommended by both the Ministry of Health and the World Health Organisation Had they gone further and correlated the findings of virus in the pharynx with the level of antibody in the blood they *might* have shown it a reliable means of distinguishing contacts who because they still carry virus in their pharynx are dangerous to the community from their fellows who, while excreting it in their fæces are past the dangerous stage of pharyngeal carriage

Is it too much to hope that they will study this aspect in the next outbreak which comes to their notice so that we can have the advantages of quarantine and at the same time inconvenience as few contacts as possible for as short a time as possible ?

Nuffield Orthopædic Centre
Oxford.

MARGARET AGERHOLM

COMPLICATIONS OF CHLORPROMAZINE THERAPY

SIR,—In their valuable article in your issue of June 4 Dr Lomas and his colleagues state that epileptic fits occurred in 10 of their 800 patients They do not give the frequency or number of fits but they say that the occurrence of fits is regarded as a contra indication to chlorpromazine Since chlorpromazine has been in use at this hospital epileptic fits have occurred in 3 patients 1 of these patients had had a leucotomy but had never had an epileptic fit before 1 patient had only had one epileptic fit eight years previously while the 3rd had never had an epileptic fit in the ordinary way but had had six seizures during a course of insulin-coma therapy

These patients were investigated electro-encephalographically after the fits. The first 2 patients had normal records. The 3rd showed an unstable alpha rhythm in the resting record. There were no changes on flicker stimulation but overbreathing caused some runs of 5 per second generalised activity and also bilateral sharp wave discharges, especially anteriorly

These 3 patients were then given 50 mg. of chlorpromazine intravenously the E E G again recorded, and the response to flicker and overbreathing observed. There was no change These patients have continued to take chlorpromazine without a recurrence of their fits. We believe that the fits might have been due to the fact that when the patients were placed on chlorpromazine the barbiturate on which they had been previously was withdrawn

At this hospital we have also carried out a series of daily direct eosinophil-counts, and all patients, with one exception, appear to have shown a significant fall after the institution of chlorpromazine therapy instead of the occasional rise observed by Dr Lomas and his colleagues Collateral tests designed to measure possible effects of chlorpromazine therapy on ketosteroid levels and water metabolism have been inconclusive.

Hill End Hospital,
St. Albans

I A SAMAD

CHILDREN IN HOSPITAL

SIR —I have read with interest your commentary (May 28) on Dr Mary Capes's World Health Organisation report on this subject.

It seems to be generally accepted that a child should not be admitted to hospital unnecessarily in view of the risk of emotional damage involved With our present-day facilities however it often is essential to admit a child to hospital, but if a method could be devised of taking hospital facilities to the child in his own home it should be possible to nurse at home many children who at the moment would be judged to be requiring hospital care

Thinking along these lines, the idea for a domiciliary pædiatric service has occurred to me involving the following main features

(1) A domiciliary visiting team, which would consist probably of consultant registrar resident and sister It would undertake the care of sick children at home It would visit daily or oftener if necessary and be on call at all times. It would undertake the same investigations, treatment, and research projects as it would if the patients were in hospital instead of their own homes.

(2) A special van or ambulance in which the team would travel It would be furnished with equipment to perform investigations and treatments such as blood-counts X ray examination, blood transfusion, and paracentesis Some procedures such as lumbar puncture could be performed in

it if the home conditions were unsuitable It would also be available at all times and be equipped with radio for easy contact in an emergency

(3) A staff of pædiatric nurses, under the charge of the sister They would care for the children, perhaps working on a shift system A very ill child, or one on special treatment such as intravenous drip therapy, would require twenty four hour attendance, several less ill children would be cared for by one nurse The child's mother would assist the nurse as far as possible, and gradually take over from her as the child recovered

The service, which would be based on the local children's hospital or ward, would be called in by the general practitioner confronted by a case which he would normally send to hospital He would resume responsibility for the case as soon as the child's condition warranted it

This scheme is intended for medical cases, but its use might facilitate the earlier discharge of surgical cases

It is a purely tentative scheme, which is no doubt capable of much modification and improvement Nevertheless, I feel that by its use many children could be spared the potentially traumatising experience of separation from their mothers at a time when they are least able to tolerate it

Edinburgh JANET HAZELL

CANCER RESEARCH

SIR,—It was startling to read Dr Burnet's letter of May 21 and his protest against the present methods of cancer research To abandon experimental methods in favour of bedside observation and to use the money saved to build hospitals would block the sources of all progress and knowledge It is false to maintain that research has " proved absolutely fruitless " The clinical picture of cancer is well known and there is nothing to be added to textbook descriptions But experimental work is of the greatest importance I need refer only to the great many discovered carcinogens (about 700) and their effect

The research of the last fifty years has yielded remarkable results, though I must admit that the practice of therapy is hobbling behind in comparison with the theory We are surely now at a stage where success is written with sympathetic chalk on the blackboard over which the lucky scientist will one day wipe a sponge Patience and assiduity are necessary Experiments on animals cannot be avoided, because every progress in our field comes from the laboratory

Düsseldorf TH OLBERT

HYPERSENSITIVITY ANGIITIS

SIR,—We were most interested to read Dr Rose's comments in your issue of June 18 It seems to us, however, that to attribute a condition such as polyarteritis to drug sensitivity, or to any cause, is not a matter susceptible to proof until sufficient observations have been recorded to be the subject of statistical analysis More frequently, indeed, opinion comes to be a matter of the most reasonable probability in the light of collected experience this being a justification, Sir, for the recording of single cases

In our patient, it seemed more reasonable to us to accept a relationship between the various and at times dramatic manifestations of drug sensitivity, and the simultaneous exacerbations of the polyarteritis which eventually proved fatal, than to postulate that the polyarteritis of whatever ætiology, was progressing quite independently

Satisfactory as Dr Rose's personal experience of cortisone treatment of over 40 cases of polyarteritis (mostly through the Medical Research Council) has been, this has clearly not been the case with our patient, nor with those of other authors quoted by us

J R EDGE
S FAZLULLAH
J WARD

North Lonsdale Hospital
Barrow in Furness

MENTAL RETARDATION

SIR,—The second footnote to Dr Alford's articl (June 18) may give rise to confusion The article doe appear to deal also with the lower grades of menta deficiency, as in the remark " when a child is born wh is obviously mentally defective " A child recognise to be mentally defective at birth is unlikely later to be i the " educationally subnormal " category

The present distinction between educationally subnormal and ineducable does, I feel, affect adversely th parents of the ineducable, and serves no useful purpose The statutory notification of the ineducable to the loca health authority labels the children unnecessarily Surely the most humane and logical procedure would b to retain such children in the school system, by makin education authorities responsible for occupation centres Support is given to this suggestion by the recent approva of the Ministries of Health and Education to the application of the term " teacher " to staffs of occupatio centres A circular letter from the National Associatio for Mental Health, dated June 13, 1955, quotes a remar of an officer of the Ministry of Education " it appear to be increasingly recognised that there is no essentia difference between education and training "

Admittedly some of the lowest grades of mentall handicapped children require institutional care, bu admission to hospital should be possible without lega procedure Amendment of the law relating to menta health—now under consideration—should abolish th artificial line of demarcation between educable an ineducable children, with resulting advantage to th mental health of the parents of the latter

Health Department,
Southampton

W P CARGILL
Deputy Medical Officer of Health

DIGITAL ARTERIES IN RAYNAUD'S DISEASE

SIR,—I have read with great interest the article b Mr Lynn and his colleagues (March 5), particularly a its appearance was almost simultaneous with that of paper of my own on the same subject[1] If the term " Raynaud's phenomenon " is restricted to patients i whom (*a*) there is no discernible primary disease an (*b*) there is no evidence of arterial occlusion, at least i the early stages, I have found, in this country, tha " Raynaud's disease " accounts for only a minority o instances of " Raynaud's phenomenon " Among th latter, there is a group of patients with clinical evidenc of structural occlusion of digital arteries and arteriographic features of the kind described by Mr Lynn an his colleagues

I would criticise their suggestion that the term " thrombotic digital artery disease " should be used in these cases This is unjustifiable in the absence of histological evidence that thrombosis is the usual mechanism of the occlusion I had used a similar term until one of my patients died a few months following clinical evidence of digital arterial occlusion the arteries of the hand were dissected and the digital arteries (communis and propria) were found to be occluded not by thrombus but by intimal proliferation Since then I have bee content to say " digital-artery occlusion, cause unknown "

Like Mr Lynn and his colleagues, I have found sympathectomy disappointing in these patients In fact, it sometimes seemed to make the condition worse. However, I do not think that arteriography is essential to distinguish structural from functional occlusion of digital arteries This can readily be done by an arterial occlusion reactive hyperæmia test performed in the manner described by Lewis and Pickering[2] In normal persons and those with functional arterial block, the fingers flush to their tips in less than five seconds after the release of the occluding cuff on the arm In those with blocked

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1 *Med J Aust* March 26, 1955 p 455
2 Lewis, T , Pickering, G W *Clin Sci* 1933, 1, 327

digital arteries there is a definite delay in flushing of the affected fingers. The findings from this test correlate very well with those of arteriography.

Baker Medical Research Institute,
Alfred Hospital,
Melbourne Australia.

A. J. BARNETT

EFFECT OF HYDERGINE ON UTERINE ACTION

SIR,—The article by Professor Jeffcoate and Mr Wilson in your issue of June 11 raises once again the important question of the ethical justification of using normal healthy patients as experimental material. One appears that in this case 59 patients in perfectly normal labour were given intramuscular injections of 'Hydergine' and another normal group of 5 were given it intravenously. They were already having routine injections of morphine and pethidine and were in no sense in need of further treatment. The hydergine was administered solely for the scientific purpose of determining its effect upon the uterus, and in a few cases of ascertaining if it had the effect of neutralising oxytocin given by intravenous injection.

In [illegible] of the cases "the treatment seemed to cause a considerable increase in the amount of pain," and in another group 6 women whose pain was increased had to be given pethidine intravenously. The conclusions drawn from the tocographic records made in a number of cases were that hydergine can induce hypertonus but that its oxytocic action is not so strong or *dangerous* as that of dihydro-ergotamine ' (my italics).

There can surely be no question but that the giving of the drug involved some risk however slight and the question therefore arises how many of us would permit our own wives to be subjected to this kind of experiment and secondly, were the wives and their husbands fully informed as to the nature of the tests and permission obtained in these cases. I feel that to clear up any possible misunderstanding some explanation on the part of the authors would be welcomed.

Camberley Surrey

M. BEDDOW BAYLY

*** Dr Bayly's letter has been shown to Professor Jeffcoate and Mr Wilson, whose reply follows.—ED. L.

SIR,—We agree that those undertaking 'clinical research' have a duty to avoid experiments which are unnecessary to the treatment of the individual patient and which carry risk of injury or discomfort. It is doubtful where to draw the line and it could be argued that some of the routine tests carried out everywhere today as part of the investigation of many patients are strictly unnecessary or that it is culpable ever to try out a new pattern of obstetric forceps. Sometimes however there is a clear need to weigh carefully the claims of advancing knowledge against the interests of the individual, and the decision to embark on a particular research project can be difficult, and its propriety a matter of opinion. Such issues could be debated at length but they are not strictly relevant to our work with 'Hydergine,' about which there appears to be some misunderstanding in the mind of Dr Bayly.

We were not experimenting in the accepted sense of the word but merely administering a substance which in recent years, has achieved a wide reputation for giving a woman a speedier and more comfortable labour. Thus hydergine and allied compounds are or have been given routinely to parturient women in certain clinics in this and other countries, and even within this last week we and we assume other members of the medical profession have received yet another postal advertisement extolling their virtues and advocating their use. We therefore applied what can be described as an accepted line of treatment designed to help the patient and the only [illegible] was an attempt to control treatment by withholding it from certain women (for which it might be more reasonable to blame us) and by recording uterine action with our external tocograph which is scientifically unsatisfactory but has the merits of depriving the patient of the risks and discomforts which accompany other methods which have a stronger appeal to the experimentalist.

Our finding that hydergine appeared to intensify rather than relieve the pain of labour in certain cases was opposite to what was expected and contrary to the claims of other observers. Moreover our observations that hydergine and dihydro-ergotamine are potentially dangerous arise *as a result* of this and similar clinical studies and were previously unsuspected. In fact, however there is no evidence that any mother or baby in our series suffered harm from their use, and the discovery of their potential dangers under conditions which guaranteed safety may help to avoid their being used harmfully under other conditions.

In short, we gave to a woman in labour a substance which medical opinion assured us was of value to the individual and free from risk. The fact that our experience did not substantiate this opinion is merely an example of an ever recurring situation in which the early exponents of a new method tend to be prejudiced in its favour by enthusiasm whereas subsequent workers uncover disadvantages not previously appreciated.

T. N. A. JEFFCOATE
J. K. WILSON

Liverpool

A BARBITURATE ANTAGONIST

SIR,—I agree with Professor Shaw and Mr McCallum (June 11) that there is some evidence that phenobarbitone is at least partly broken down in the body. My main reason for believing that any such breakdown products do not contribute significantly to blood phenobarbitone levels estimated by ultraviolet spectrophotometry is that I have identified phenobarbitone by paper chromatography in 5-ml. samples of blood taken from patients as long as ten days after ingestion of the drug. On the other hand, I have not been able to demonstrate by this method the presence of spots in any other position than that occupied by phenobarbitone. It is unlikely on theoretical grounds that breakdown products would travel on paper chromatograms at the same rate as the parent substance.

A further point is that the rate of disappearance of phenobarbitone from blood is slower but of the same order as that of barbitone. It is generally agreed that barbitone is stable in the human body.

Professor Shaw and Mr McCallum do not agree that "the worth of new barbiturate antagonists can be evaluated by a measurement of drug levels in the blood." They add that "the only test is the pragmatic one of a lessening of the duration of coma and the mortality rate."

In the light of these statements I have studied with great interest the recent paper by Professor Shaw and his colleagues.[1] The case notes show that ββ methyl ethyl glutarimide (N.P.13) and 2:4 Diamino 5 phenyl thiazole hydrobromide or hydrochloride (D.A.P.T.) do indeed have analeptic activity especially where short-acting barbiturates are concerned. But in 10 cases of prolonged coma (9 of which were due entirely or in part to phenobarbitone) the authors appear to have been unable to restore consciousness without risk of inducing convulsions. In 7 cases for whom the amount of phenobarbitone ingested is recorded my calculations (which assume a body weight of ten stone in each case) lead to the conclusion that only 2 (cases 18 and 21) regained consciousness earlier than might be expected without analeptic therapy—i.e. blood phenobarbitone level above about 5 mg. per 100 ml. During the period of coma these patients are said to have been maintained in the "safe state "—but how safe is a state bordering on convulsions? This is a question which those familiar with the effects of picrotoxin have asked for many years

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[1] Shulman, A., Shaw, F. H., Cass, N. M., Whyte, H. M. *Brit. med. J.* May 21, 1955, i, 1238.

The specificity of a barbiturate antagonist should be proved in cases of poisoning due to the long acting barbiturates for, in my opinion, prolonged coma in such patients is usually due entirely to the presence in the body of unchanged barbiturate (unless such breakdown *products as may occur are also biologically active*) and not to the effects of shock and anoxia

The London Hospital, E 1 J T Wright

TEACHING DEAF CHILDREN

Sir,—As pointed out by Mrs Ingall in your issue of June 11, there seems still to be a certain amount of confused thought about the stage at which special education of the young deaf child should commence It cannot be sufficiently stressed that early lip reading training and the use of any available hearing should start *as soon as the diagnosis is made* Moreover, this diagnosis must be made at the earliest possible moment after birth, or after the child has suffered from any illness which has produced damage to the hearing mechanisms

On the other hand, the 1944 Education Act should not be regarded as an educational textbook Section 34 of this Act lays down merely that handicapped children may be "ascertained" at the age of two and can be afforded facilities for special education from that age if the local education authority thinks fit Since the diagnosis of congenital deafness can be made in the otherwise normal child in the majority of cases by the age of twelve months, and is often made by their mothers long before this, the work of a number of hospital clinics and local health authorities with these patients is gratifyingly on the increase

The tendency to postpone a decision about the disability arises from the misconception that the necessary training for these young children involves admission to a special residential school This is completely inaccurate, for where the home conditions are suitable the parents can give more help by home training under the guidance of a teacher of the deaf than can be given to the child in a nursery school It is more economical of teaching man power and avoids the psychological consequences to the child due to its removal from the sense of security provided by home and parents

Eye Ear and Throat Hospital,
Murivance, Shrewsbury E N Owen

FOOD IN MENTAL HOSPITALS

Sir,—Having devoted a considerable time to nutritional studies in a mental hospital during the past few years, I greatly welcome Mr Harington Hawes's article of June 11 Most of us will agree with his criticism of present day catering arrangements, and especially the long wait between the early meagre supper and next morning's breakfast

There are several aspects which can be raised in discussing food in mental institutions Our data gained in a hospital with over 2500 beds are being evaluated at present and no ultimate conclusions can be drawn yet It can, however, be said that (at least in the hospital in question) the overall nutritional state of the patients was satisfactory and frank nutritional deficiencies were only rarely found, although some of the patients had been in hospital for several decades Indeed some of the worst acute deficiencies were found in newly admitted patients

Our preliminary publications[1] demonstrated low carotenoid values and low vitamin A and vitamin C reserves among the hospital population, and I therefore would support Mrs Pulvertaft's suggestion (June 18) of spending any additional available funds on fruit, salads, milk, and cheese The detailed results of ou studies will be published shortly

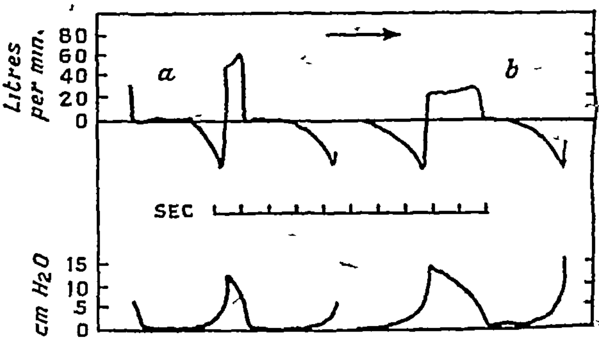
London, W 1 Z A Leitner

ARTIFICIAL RESPIRATION BY INTERMITTENT POSITIVE PRESSURE

Sir,—Dr Spalding's article of May 28 rightly stresse *the way in which the degree of the distension of the lung* within the thorax depends upon the air pressure applie to the air passages, provided that the air passages ar not blocked and that there is no undue rigidity or resis tance of the chest walls

I feel, however, that his conclusion—that prolongatio of inspiration beyond 1 5 sec provides little useful increase in tidal air—may be open to the misinterpretation tha this figure is a physiological constant Surely, it must depend as much upon the machine as upon the patient

If one considers a point 0 1 sec after the start of inspiratio (fig 5*b*) it will be seen that the pressure close to the externa end of the endotracheal tube had already risen to 10 cm. H_2O The cause of this pressure must have been the resistance o the "airway" (endotracheal tube, air passages, &c) to the flow of air, for, so early in inspiration, the elastic restraint o the lungs in thorax must be very small From fig 3*b* we can see that the rate of flow of air must have been 40–60 litre per min. at this instant When such instantaneous rates o flow are available, it is not surprising that a respectable tidal volume can be fed into the lungs in 1 5 sec or even less



Two sample inspirations using a respirator set to change to expiratio at above 13 cm H_2O

Dr Spalding's machine evidently had the very good characteristic of being able to supply 40–60 litres per min. against 10 cm H_2O back pressure, even when set so that its maximum pressure could not exceed 15 cm H_2O Unfortunately, many respirators are not so good and when they cannot provide air flow so freely it is surely no longer true that prolongation of inspiration beyond 1 5 sec provides little useful increase in tidal air

The accompanying figure shows flow diagrams of two sample inspirations using a pressure sensitive respirator set to cut off and change to expiration at about 13 cm H_2O The lower traces are of the pressure near to the external end of the endotracheal tube In flow tracing *a*, air flowed into the lungs at about 60 litres per min at the start of inspiration and continued at about this rate until 0 8 sec later when (from the area of the trace) about 700 ml. tidal volume had been insufflated and the pressure due to distension of the lungs amounted to 13 cm. H_2O, so that inflation ceased In tracing *b, in order to simulate many less satisfactory* respirators, the maximum flow was restricted to about 35 litres per min At the end of 2 sec, air was still flowing in at about 30 litres per min but since (from the area of the trace) some 750 ml had been insufflated, the distension of the lungs had resulted in a pressure of 13 cm H_2O and inspiration ceased In the latter case, useful tidal air was obviously being added at 1 5 sec. and beyond

Even more exaggerated effects can be shown but I wished to work within practical limits There is a respirator on the market which cannot deliver air faster than 15 litres per min.

The pressure curves corresponding to the flow diagrams are very different from any Dr Spalding shows This must have been because the resistance of the “ airway ’ was less in my patient than in Dr Spalding’s Again, if we consider a point 0 1 sec after the beginning of inspiration air was flowing through the airway at 65 litres per min., but the pressure driving it was only 3 cm. H_2O Such possible variation in the airway resistance in healthy people is surely another reason why Dr Spalding s figure must not be misinterpreted as being a physiological constant.

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[1] Leitner, Z A *Brit J Nutr* 1952, 6 viii Leitner, Z A. Moore T, Sharman I M *Ibid*, p x, *Ibid*, 1954, 13 xi

I agree with Dr Spalding that it is desirable that inspiration should be as short as possible and to this end, the respirator should be able to feed in a lot of air quickly The practical limit to the speed of inflow at the beginning of inspiration will be the resistance of the airway and the highest pressure which is considered permissible at the external end of the endotracheal tube For a given peak or cut off pressure respirators vary a good deal in their ability to deliver big flows against back pressure

Dr Spalding rightly underlines the importance of the short inspiratory phase in maintaining a low mean intrathoracic pressure and thus avoiding embarrassment to the circulation It is worth mentioning that this end can also be served very effectively by applying suction during the expiratory phase

Royal Victoria Infirmary
Newcastle upon Tyne

E A. PASK.

PERIODIC SYNDROME

SIR,—With reference to Dr Reimann’s letter last week on cyclical vomiting his work on recurrent neutropenia is well known With Dr C T de Berardinis he has described[1] the condition and similar cases have been seen in this country[2] Early in my research I thought that I had met with some myself The patients had recurrent pyrexia abdominal pain and neutropenia Some of them had arthritis and splenomegaly However the work of Barrett and Rickards[3] led me to suppose that they may have been suffering from brucellosis despite negative agglutination tests Dalrymple Champneys[4] has pointed out that this condition may last for as long as forty years It is most important in such cases to perform a brucellin skin test, and to determine whether this provokes a rise in titre of agglutination

Bath.

HUGH R E WALLIS

TREATMENT OF CHRONIC AMŒBIC DYSENTERY

SIR,—I have read the article by Lieut Colonel Inder Singh (March 12) and the subsequent correspondence (March 20 and June 11) with interest, but I have been struck by the complete absence of any mention of clinical findings. It has always struck me that the essential difference between amœbiasis, a disease, and amœbic infestation a harmless parasitism is that in the former there is always a massive invasion of the gut wall, which is easily detectable clinically by a gross thickening and tenderness of the cæcum and colon If this is present whatever the stool findings may be a course of systemic amœbicides must be given which if there is any liver tenderness on percussion should include chloroquine

I wish it were possible to believe as Dr Andrade (June 11) implies that one cannot contract the disease from one s own harmless infestation It seems to me more likely that the parasite after ingestion is forced to feed on the less favourable pabulum of bacteria because of a high host resistance; if however this becomes lowered there is an immediate widespread penetration into the gut tissues by the amœba in whatever form it may be multiplying at the time For this reason I think that if cysts are found without evidence of the disease, they are best killed and a week s course of one of the bisarsenates usually seems adequate for this purpose For those in whom attacks of the disease are common—i e , those with a low natural resistance—it would seem that a prophylactic amœbicide should be possible and I am now trying a combined tablet of bisarsenate with chloroquine, two twice weekly

I believe that as the clinical diagnosis of this disease is comparatively easy too much attention need not be paid to the stool findings the difficulties of which have already attracted a wide literature[5]

Calcutta.

ROGER LANE

HEROIN

SIR,—Following the letter from Mr Southwood in your issue of June 11 deploring the action of the Government regarding heroin, you add an editorial annotation in which you refer, in perhaps a somewhat misleading manner, to the report of the representative meeting of the British Medical Association in the same issue Would it not have given a fairer view of the question to have stated that the meeting passed a resolution protesting against and asking for a reversal of, the ban on the manufacture and use (but not the export) of heroin ?

Moreover the same representative meeting passed a resolution wishing it to be made known that the B M.A had not been consulted or asked for an expression of its views in any way on the question of the abolition of the manufacture and use of heroin

Nor was the question of a ban on heroin referred to the Royal College of Physicians Had it been there is little doubt that a majority of fellows would have given advice quite different from that tendered by the Central Health Services Council which certainly cannot be regarded as representative of those in active medical practice

Incidentally had you Sir read the letter in *The Times* of May 18 from members of the staff of University College Hospital Medical School it would have been obvious that any action taken in this country could have no effect on heroin addiction, in this country or elsewhere

London S.E 1

J J CONYBEARE

*** An editorial on this subject appears on p 1311—ED L

STERILISATION OF BLANKETS

SIR,—The paper by Dr Blowers and Dr Wallace in your issue of June 18, as evidence of interest in the sterilisation of hospital blankets is very welcome Contrary to the opinion expressed in this paper Fixanol C has not an unpleasant odour does not stain the blankets and it does dissolve in water—perhaps not easily but sufficient to give a dilute solution which is all that is necessary We were the first to recommend the use of Lissapol to remove traces of soap from blankets to be treated and to act as a cleansing agent to replace soap As Dr Blowers and Dr Wallace state, soap antagonises the bactericidal effects of quaternary ammonium compounds we also mentioned this effect in our paper in your columns last year[6]

St Margaret’s Hospital
Epping Essex.

FRANK MARSH

ANTI-HISTAMINES AS HYPNOTICS

SIR,—To depart completely from the basic technique of the trials described in your annotation of May 7 might it not be much more conclusive to carry out tests, for hypnotic action in the subject who *wishes* to be wakeful ? That is, in any normal person (the nearer normal the better) during the day while at work

I suggest that the omission of breakfast and the substitution of the top dose of any anti histamine drug with a reputation for marked soporific side action will leave the investigator in no doubts whatever as to its activity in this direction Placebos could be included in such tests the preoccupation with work mitigating any purely psychogenic response

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[1] Blood, 1949, 4 1109
[2] Moncrieff A *Arch Dis Childh* 1951 26 434
[3] Barrett, G M Rickards, A G *Quart J Med* 1953 22 23
[4] Dalrymple-Champneys W *Lancet* 1950 i 429
[5] Lane R, *J trop Med* 1951 54 195
[6] Marsh F Rodway H J *Lancet* 1954 i 125

If it is wished to place the trials on a scientific basis, then experimental subjects could perform standard tasks for evaluation by independent observers, here it might be desirable to add a drug of known hypnotic value, for purposes of qualitative comparison

Port Elizabeth
South Africa
R E HOLMES

BY ANY OTHER NAME

SIR,—I am a philatelist and therefore interested in the details of printing processes In order to elucidate the problems which arise it is often necessary to gaze at some thousands of copies of the same stamp Here I am faced with the same sort of problems (mentioned in your leader last week) that beset the chest radiologist I am looking for minute flaws, sometimes obscured by postmarks He is looking for similar defects sometimes obscured by rib shadows, &c

The great difficulty is to focus both mind and eye on each part of the stamp or film in turn This is very tiring and one tends to overlook the areas in which flaws are less common and to miss them altogether where the design is complex Moreover, the mind looks for the usual type of flaw and is apt to miss the unusual

I am not sure what the remedy should be I think one should have the normal in mind—which will happen after looking at 100 or so films or stamps—and should then strive to focus in turn up one side of a stamp or film, down the middle, and up the other side But I still have much the same error rate as the radiologist

Sevenoaks, Kent
GORDON WARD

SWEETS AND DENTAL CARIES

SIR,—Once again the medical profession is fighting a (? losing) battle against vested interests

Cigarette manufacturers won the fight against prevention of bronchial carcinoma, and now sweet manufacturers are considering how further to increase their enormous sale of sweets, which is already the highest per head in the world

One only has to live near a sweet shop, and watch children coming and going there all hours of the day, to realise how hopeless the fight is for prevention of dental caries

Unless there is an active press campaign, assisted by explanatory talks by dental officers in schools and clinics, and medical practitioners in surgeries, homes, and elsewhere, pointing out the danger of sucking lollipops, toffees, and suchlike, the number of dental casualties will go up and up

What about a high purchase tax on "dangerous" sweets ?

Nottingham
G FIELDING

DANGEROUS COTS

SIR,—I have a certain amount of sympathy with the views of the cot manufacturers which you criticise in your annotation of June 18 Those who work in children's hospitals will agree with me when I say that only eternal vigilance can prevent accidents If not watched children will pour soup over themselves, eat their coloured pencils, push buttons up their nose, and undo their bandages I know of one fever hospital where the superintendent gave instructions that cot sides must not be put up because when children climb over them (and they do !) they have so much further to fall At another, no restrainers are allowed because some years ago a child was killed by getting entangled in one Narrowing the distance between bars may prevent one type of accident, but accidents are not caused so much by faulty equipment as by the restlessness of children exploring their world with great determination and little sense They need conscientious nurses to watch them whatever type of bed they are in

There is a further point I should like to make Our toddlers' ward at present houses 20 children between three and five, none of whom could be squeezed through the bars of his cot in the manner you describe and most of whom wear, in addition, plaster jackets or various types of splint Yet, I am told, the Ministry circular leaves our administrative staff no choice but to change our present cots for new ones at the expense of several hundred pounds To issue a circular calling attention to the danger of one type of child in one type of cot is one thing, to issue instructions altering every cot in every hospital in the country quite another

King Edward VII
Orthopædic Hospital
Sheffield 6
E G HERZOG,
Surgeon Superintendent

SIR,—I suggest that if the bars were placed horizontally the accidents could not occur

London, W 1
HAROLD KISCH

*** But would the child stay in the cot ?—ED.L

Obituary

DONALD BREADALBANE BLACKLOCK

C M G, M D Edin, D P H, D T M

FROM 1929 until he retired in 1945, Dr Blacklock filled with distinction professorial chairs at the Liverpool School of Tropical Medicine But he was never content to direct operations on the tropical front, and he continued, on arduous tours to unhealthy spots, his service for those who work in tropical climates

He was born in 1879 at Oban, the son of the Rev John Blacklock From Fettes College he went to the University of Edinburgh, where he played forward for the Edinburgh Wanderers and cricket for the university After he qualified in 1902 he practised for a few years in South Africa, but on his first leave home he met Warrington Yorke, then a research assistant at the Liverpool School of Tropical Medicine's laboratory at Runcorn From this chance meeting there grew a close friendship and scientific partnership, for Blacklock was so fascinated by the work he saw at Runcorn that he threw up his promising South African practice to join the staff of the school In 1907 he took the D P H, in 1909 the M D, and in 1911 the D T M The same year he was appointed research assistant at Runcorn, and he continued to work there until 1914, when he was appointed director of the laboratory and later lecturer in parasitology to the school During these years he produced some twenty papers on trypanosomiasis, most of them in his own name but some in joint authorship with Warrington Yorke One of these papers recorded the important discovery that *Trypanosoma cruzi* could develop to the infective stage in the bed-bug But most of his published work dealt with the morphology of trypanosomes and, particularly, with the discovery of posterior nuclear forms of *T rhodesiense*

In 1914 Blacklock and Warrington Yorke, with the school's 32nd expedition, visited West Africa to arrange for the site of the Sir Alfred Lewis Jones Research Laboratory While in Sierra Leone they studied the breeding-places of *Glossina palpalis* and the species of trypanosomes transmitted by the fly to man and his domestic stock By the time the expedition returned to England war with Germany had broken out, and Blacklock joined the R A M C, to serve in the Dardanelles and France until 1916, when he returned to look after tropical cases at the school, which had been converted into a hospital While he was stationed at home he went on with his research and he collaborated with Stephens, Yorke, and other colleagues in papers on the treatment of malaria These papers, though now obsolete, were at the time of their publication, highly important, for they showed the Army authorities how best to control this disease which so greatly interfered with operations in the field With Warrington Yorke he also studied the periodicity of the microfilaria of *Wuchereria bancrofti*

In 1921, when the Sir Alfred Lewis Jones Research Laboratory was opened by the Liverpool School at Freetown, the University of Liverpool appointed Blacklock director of the laboratory and professor of tropical diseases of Africa During the next eight years, while he established the laboratory on a firm footing he covered the diseases of Sierra Leone on behalf of the government, and directed important research, much of which was achieved only by travelling up country under primitive and trying conditions

His investigation of an outbreak of beri beri in the Freetown jail proved the cause to be the faulty preparation of the rice a discovery which eliminated this long-standing cause of sickness in the prisons During a tour in the northern province of Sierra Leone he observed that in this area a high proportion of cases of goitre were associated with heavy fæcal contamination of the drinking-water In entomology his main interest was the breeding places of the local anophelines and as a result of his investigations anti malarial measures in Freetown and its environs were put on a more scientific basis He also collaborated with his wife Dr Mary Blacklock, in a comprehensive study of the tumbu fly In the course of this investigation he observed evidence of resistance developed by the host against this parasite and with Prof R M Gordon he published papers on this aspect of metazoan immunity His contributions to protozoology included his studies on malaria in the chimpanzee, and again with Professor Gordon on placental malaria. In helminthology Blacklock added much to our knowledge of West African schistosomiasis, and completed, in 1927, the proof that *Onchocerca volvulus* was transmitted to man by *Simulium damnosum* —a pioneer investigation which, for the first time allowed methods of control to be applied to a disease which has been a widespread cause of blindness both in West Africa and in Central America. He was also interested in that strange disease blackwater fever, and he showed that the transfer of blood from the patient to a normal person did not reproduce the infection. Those who knew Blacklock will correctly surmise that this somewhat risky experiment was performed on himself and a colleague recalls appreciatively that he had the discrimination to choose a bishop as his donor

In 1920 he returned to Liverpool to succeed Warrington Yorke in the Walter Myers chair of parasitology, which he held until 1934 when he was appointed to the newly established chair of tropical hygiene But though this chair was now in England, much of his work still lay abroad. In 1935 with a Leverhulme fellowship he visited China, Malaya, Burma India and Ceylon to study the techniques of rural hygiene used in the tropics, while his wife, who held a similar fellowship, made a special study of the health of the women and children Housing in relation to tropical disease was another subject which interested him and he was a member of the Colonial Housing Research Group

During the late war, Freetown was a great convoy centre for war-time shipping and it was vitally essential that this base should be in constant use. Unfortunately the mosquito proved an even more formidable foe than the enemy the crews and the troops on board the ships at anchor in the harbour, as well as the men stationed on shore, were exposed to the bites of mosquitoes and became infected with malaria to an extent which threatened to disorganise the whole convoy system. In this crisis the authorities approached the Liverpool School of Tropical Medicine and Blacklock, now nearly 65 with the rank of surgeon captain R N V R sailed again to the discomforts of West Africa. The success of his work there was soon shown by the fall in the sickness rate which followed the adoption of his recommendations and in 1912 he was appointed C.M.G Besides this well earned honour he also enjoyed the rare distinction of having served his country with the rank of captain in the Army in one war, and captain in the Navy in the next. In 1914 at the request of the Government he again visited West Africa

Blacklock s clear and incisive mind made him an excellent lecturer and the many editions of his *Guide to Human Parasitology* written with T Southwell, bear witness to his powers as a teacher In 1945 he retired from his chair after serving the Liverpool School for thirty four years, and retired to Cornwall He died on June 10 at his home at Mawnan

R. M G writes: Blacklock s acknowledged position as a leader in tropical medicine was not the result of personal ambition for he was the most modest and least self-seeking of men; rather was he carried to the front of scientific research on the tide of his own discoveries and in his advance he brought with him many younger and less experienced colleagues There are today a host of workers in tropical medicine who owe their positions to the early training they received from him, for he had the power not only of imparting knowledge but of inspiring enthusiasm and turning dull routine into a fascinating preliminary struggle with a worth while problem

' Blacklock travelled widely and studied tropical medicine in every part of the world but his name will always be associated most closely with his work in West Africa, particularly in Sierra Leone, a colony from which he did more than any other man to remove the stigma of the white man s grave It was in Sierra Leone that he carried out the manifold researches in entomology and parasitology which are recorded in his published works It was in Sierra Leone that he made the discovery which ranks high in the annals of tropical medicine, of the transmission of *Onchocerca volvulus* by *Simulium damnosum* and it was to Sierra Leone that he returned during the late war to solve the problem of malaria control in Freetown.

Despite his reserved manner, he was universally popular and he will be mourned by many friends in many parts of the world and in every rank of life The reason for this unsought popularity was not far to seek he was a fine man in every sense of the word fine in body, fine in intellect, and possessed of a wonderful power of ignoring the worst and perceiving the best in his fellow man

Professor Blacklock married in 1922 Mary Georgina, daughter of George Matthew Thompson M.D., of co Derry who survives him As his student and later as his colleague in West Africa, she shared in much of his research.

REDCLIFFE NATHAN SALAMAN

M.A M D Camb., F R.S. J.P

Ill health forced Redcliffe Salaman to give up medicine four years after he qualified, but it remained within the range of his flexible scientific interests As director of the Potato Virus Research Station of the University of Cambridge he made important contributions to our knowledge of virus diseases and he continued to urge the need for closer understanding between the pathologist and the plant breeder

(Walter Stoneman

He was born in 1874, one of the twelve children of Myer Salaman a City merchant. He was educated at St. Paul s School and at Trinity Hall Cambridge, where he studied under Michael Foster Gaskell and Macalister After taking a first in the natural sciences tripos he entered the London Hospital He began to do research even before he qualified in 1900 and after holding a house-appointment under Henry Head he continued his postgraduate studies and research at Würzburg and Berlin On his return he was appointed director of the pathological institute at the London Hospital and pathologist to the Zoological Gardens. But in 1904 he developed pulmonary tuberculosis After eighteen months in Switzerland he returned to England restored to health, but decided to spend his life in the country He accordingly settled at Barley in Hertfordshire where he began his genetic and agricultural researches His special interest was the potato plant, and in 1920 he published the results of many years private investigation in his book *Potato Varieties* The same year he persuaded the late Sir Daniel Hall and the Ministry of Agriculture to found a research station at Cambridge to investigate the virus diseases of the potato He became director of this institute and soon afterwards with R H Le Pelley published a description of the virus latent in all potato plants of the King Edward variety which he named the Paracrinkle virus. "This discovery," writes K. M. S., "gave great impetus to the study of latency in plant viruses, and is still one of the strongest pieces of circumstantial evidence for the endogenous origin of some plant viruses. By means of careful testing and selection he also built up a nucleus stock of virus-free seed potatoes which were grown under insect-proof conditions in the Cambridge glass-houses. From this stock small quantities of each variety were multiplied up each year out of doors under conditions of strict isolation from all other potato plants. Much of this work was done on a small island off the west coast of Scotland where there were no other potatoes being grown. These nucleus potato stocks are still in existence and their propagation and care are now under the direction of the National Institute of Agricultural Botany at Cambridge. This idea of raising virus-free stocks of potatoes with a view to improving the yield and quality of the crop generally has now been copied in many other countries. Salaman's interest, however, was more in the potato plant than in viruses, and he spent much time in breeding new potato seedlings for resistance to potato blight, *Phytophthora infestans*."

In 1935 he was elected F.R.S. In 1939 he retired from his appointment to spend the next years writing *The History and Social Influence of the Potato* (1949) in which he traced the history of the plant in relation to social and economic conditions.

A man who was thus ready to point out the wider implications of the virus diseases of plants could not fail to have many interests outside his own research, and he had won respect on the magistrates' bench as well as at the laboratory bench. He became a J.P. for Hertfordshire in 1901, and for twenty-three years he was chairman of the bench.

He also gave much devoted and discerning service to the Jewish community, of which perhaps the most important was his chairmanship of the Jewish Committee for Relief Abroad which was founded in 1943. Of this personal side of his life, S. W. writes: "I first met Redcliffe Salaman some 20 years ago. He was an unusually good-looking man, an aristocrat to the finger-tips, quite uninhibited, always saying exactly what he thought without care about the consequences. I never knew him as a scientist and often wondered how a man of such obviously high intelligence and delicate sensibility could have given up the study of man to devote himself to the potato; but he was very good at potatoes. Our common interest at the time was the plight of the scientists, scholars, and doctors who were being driven out of Germany by the Nazi persecution. Salaman devoted every ounce of his energy to this cause. He took great pains to get to know the displaced workers well and used all his influence to find new opportunities for them at home and overseas. He was a pretty good judge of real ability. I remember him saying of one young and relatively unknown biochemist that he was an obvious future Nobel prize-winner; and so he proved to be, and much else besides. What stirred Salaman to action was not only his abiding sense of loyalty to his fellow Jews, who constituted the majority of the victims, but the feeling that the Nazis' behaviour was an affront to all the standards of decency and humanity for which he stood. His other constant love was the Hebrew University of Jerusalem. Though no man was more proud than he of his alma mater, Cambridge, or more touched by the honours it gave him, yet he always referred to the Hebrew University as 'my' university. He had an unlimited faith in the service it would one day render to the Jewish people, the Middle East countries, and all mankind. He put all his wisdom, integrity, and practical experience at the disposal of its board of governors and did much to steer the university safely through its early critical years. He kept in constant touch with all its problems, and until his last illness was willing to see anyone or go anywhere on its behalf if he was told that he could help. Salaman was not a man with whom you could easily become intimate; he was probably more emotional at heart than he was willing to let others know. But he was greatly touched by the honorary fellowships which both his old college and the Hebrew University bestowed upon him during his illness, for he recognised them as tokens that his devotion over many years was fully recognised and appreciated."

Dr. Salaman was twice married. His first wife, Nina, daughter of Arthur Davis, who died in 1925, is still remembered for her translations of Hebrew poetry. They had six children, of whom two sons are doctors. Dr. Salaman is survived by his second wife, Gertrude, née Lowy. He died on June 12 at his home at Barley.

CHARLES ERIC RHODES

M.B. Lond.

Surgeon Lieutenant Rhodes lost his life in H.M. Submarine *Sidon* when she sank after an explosion in Portland Harbour early on June 16. He was medical officer of H.M.S. *Maidstone*, the depot ship alongside which the *Sidon* was lying, and he boarded the submarine with the first rescue party. In difficult circumstances he got some of the wounded to safety. Shortly before the *Sidon* sank he went back to help the others, and he was not seen again.

He was born in Lancashire in 1928, the son of Mr. and Mrs. E. C. C. Rhodes of Bramhall, Cheshire, and was educated at Cheadle Hulme School and Wrekin College. He entered the London Hospital Medical College in 1946, and he qualified in 1952. He was house-physician at the London and house-surgeon at Harold Wood Hospital before he joined the Royal Naval Volunteer Reserve.

J. R. E. writes: "Few men during their years at the London have been more widely known, or more liked and respected. It was impossible not to like someone so obviously happy, enthusiastic about so many things, active in so many ways, and so completely unselfish. He was respected because with all his cheerfulness he was quiet and unassuming, courteous and kind, with sound and fair judgment. He inevitably gave more to the community than he took from it, and his influence was widely felt and good. It was typical of him that at a time when the hospital rugby XV was suffering from a clash of personalities he solved the problem by efficient and tactful service as non-playing secretary. To do so he gave up his own pleasure in a game which he greatly enjoyed, though his poor sight prevented him from being a first-class player.

"In his favourite sport, however, he achieved eminence. Not only United Hospitals, but the Royal Ocean Racing Club and sailing clubs in many parts of the country knew Eric as an experienced helmsman and a delightful companion. Qualification and house-appointments brought a halt to sailing, but his love of the sea made him determined to fulfil his National Service with the Navy. He was within a few weeks of completing it when he gave his life in an act which by its courage, unselfishness, and efficiency was characteristic. The tragedy of the unfulfilled promise, of the loss to medicine, of one who possessed complete integrity and the ability to lead by personal example, is only tempered by the knowledge that he achieved much, and in his end achieved greatness."

He leaves a widow and a daughter born a few weeks ago.

DR. R. A. LYSTER

J. B. G. S. writes: "In your obituary there is no mention of Dr. Lyster's appointment as lecturer in forensic medicine and public health at St. Bartholomew's Hospital. He was a first-class lecturer and made his lectures extremely fascinating and clear. He prepared most useful synopses which students could retain and which contained all the salient points at issue. He was able to illustrate his teaching from vast experience and was evidently a diligent reader of the Press. A frequent remark of his was 'I have a cutting here,' in order to reinforce the point he wished to make. He had a pleasing sense of humour and he told his audience that he did not wish to turn them into 'a set of amateur sleuths'. He made plain the various 'grave risks' the practitioner was likely to encounter in his daily work. He had a dignified bearing, he delivered his lectures with an articulation that will always be recalled by those who heard them. One felt the room listening to statements that had an ex-cathedra authority about them. Although he was not an old Bart's man by training, he was one of many distinguished teachers of which Bart's has always been the proud possessor."

Notes and News

OBSTETRIC MEDICINE RESEARCH UNIT AT ABERDEEN

An obstetric research team has been working under the direction of Prof. Dugald Baird in Aberdeen during the past seven years. To further this work the Medical Research Council has agreed with the University of Aberdeen and the North Eastern Regional Hospital Board Scotland, to form a unit for research in obstetric medicine under the honorary direction of Professor Baird

The Scottish Hospitals Endowment Research Trust has promised a substantial grant to the university for the construction of a building adjoining the Aberdeen Maternity Hospital to house the unit The administration of this building will be arranged jointly by the University and the Aberdeen Special Hospitals Board of Management The building will provide laboratory facilities and beds for patients requiring special investigation whose treatment can thus proceed without interruption.

The unit will continue long term research into problems of maternity using a combination of epidemiological, clinical, and laboratory methods of investigation The term "obstetric medicine" in its title recognises the fact that general health problems, of the type which are the concern of the research physician have become as important as the surgical aspects of obstetrics.

EYE INJURIES IN BOXERS

At a meeting of the honorary medical officers of the London Amateur Boxing Association on May 24 under the chairmanship of Dr J Sharp Grant Eye Injuries were discussed by Mr A. Rugg-Gunn.

Mr. Rugg-Gunn expressed the opinion that no-one suffering from any form of epilepsy should be allowed to box and recalled that patients with squint associated with amblyopia often had an electro-encephalographic tracing similar to that of epilepsy The eye he said was slung well behind the orbital rim and rested behind on a fatty cushion, the most vulnerable part being its temporal aspect, especially in adduction. The orbital rims of hard compact bone were seldom fractured but fractures in the neighbourhood of the inner canthus—e.g., the nasal bone and the naso-maxillary process—were not uncommon The commonest eye injury in boxing was "a black eye" which was rarely serious unless associated with splitting of the upper eyelid or a wound in the neighbourhood of the canaliculi Corneal and conjunctival abrasions might occur with lid injuries Subconjunctival hæmorrhages might arise from orbital hæmorrhages as well as from rupture of conjunctival vessels. A direct blow might rupture the pupillary sphincter muscle and produce hyphæma and subconjunctival hæmorrhages Rupture of the sphincter may cause permanent mydriasis and should be treated immediately with pilocarpine or eserine drops. Transient paralyses of the extra-ocular muscles causing diplopia sometimes followed hæmorrhage into the muscle substance As a rule however paralyses of these muscles were secondary to head injuries and were serious Naturally accuracy of hitting and timing of blows were grossly disturbed. A direct blow on the eye in the eyes-front position might cause serious internal injuries The elastic cornea was dented and waves of force were transmitted backwards through the media displacing momentarily the iris and lens, affecting all diameters of the eyeball, but impinging with maximum force at the posterior pole or macula. Rupture of the choroid possibly multiple and rupture of the retina (less common) might be produced These stress effects constituted so-called concussion firstly temporary vasoconstriction in the macular area, giving rise to ischæmia, and secondly, owing to the anoxia release of histamine-like substances which produced local vasodilatation œdema, and hæmorrhages. Detachment of the retina was relatively common in professional boxers and was often bilateral. Usually its onset was delayed When the onset was immediately after a blow this had probably coincided with temporary obstruction of the venous outflow from the choroid—e.g., through holding the breath—so that the overlying retina was temporarily stretched at the moment of impact Myopes were more vulnerable than others Hæmorrhage into the vitreous disorganising this locally might produce a strand-like opacity which was sometimes anchored at one end to the retinal surface Sudden movements of the eye might pull on the retina at the point of attachment and cause a tear and retinal detachment and this might happen months later Blindness in boxers was usually due to retinal detachment

OLD PEOPLE IN WELFARE HOMES

At the conference of the Association of Hospital and Welfare Administrators on May 25[1] Mr C R Pennell the association's president expressed grave concern that aged and infirm patients were being accommodated in welfare homes and looked after by staff who were not trained nurses. At one large welfare home he had visited some 70 of the people needed nursing care They could not go to an adjoining hospital because there was no room, and Mr Pennell added the local authority could not or would not employ nurses There had been some 40 doctors at this establishment during the first three months of this year But Mr Pennell acknowledged that many local authorities had made vast improvements in their accommodation for old people In fact he said there are cases where lavish might be the correct word to use and sometimes some of the old people may feel a little uncomfortable at being made too *comfortable*

MEDICAL RECORDS

At an exhibition held in London last month by the Association of Medical Records Officers various hospitals had their own stands Charing Cross Hospital gave a helpful exposition of checks and controls over the movements of case notes and also showed how the cards forming the waiting list are afterwards used as admission cards and finally as an index to the files, thus reducing repetitive clerical work. Among the Southend-on-Sea Hospital practices which were illustrated was pre registration of new outpatients, whose time at the clinic is saved by sending them a form to complete at leisure in advance and return by post The numerous other hospital and commercial exhibits included such subjects as storage outpatient appointments medical correspondence and relations between patients and staff A special stand indicated the scope of the educational work undertaken by the Association of Medical Records Officers, including the holding of examinations on a wide syllabus and publication of a quarterly *Medical Record*

As a visual means of presenting a variety of hospital techniques for the consideration of others facing similar problems in their own hospitals and clinics, the exhibition proved a useful innovation

PRESSURE PADS FOR ULCERATED LEGS

The rubber pads ordinarily employed for applying additional local pressure in the compression treatment of ulcerated legs have disadvantages which discourage their general use First, sponge rubber as usually obtainable is tough and springy and can produce a deep dent in the leg Secondly the pads have to be individually cut to size and carefully skived—the latter a tedious affair and inconvenient in a large and busy clinic

Dr Stanley Rivlin of the London Varicose Clinic points out that in practice such pressure is required chiefly in the later stages of healing—when the ulcer has contracted to the size of a half-crown and has either bumpy edges or raised central granulation tissue—and for this reason a pad of standard size will be found appropriate in most cases. To Dr Rivlin's specification the medical division of the Scholl Manufacturing Company have evolved moulded latex foam pad 8 cm. square of "unbelievable lightness, texture and porosity" which he has found admirably suited to the purpose

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[1] *Manchester Guardian* May 26 1955

Their light weight, he says, ensures soft though firm pressure, while the permeable cellular structure allows healing without maceration

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University of Sheffield

The council has made the following appointments

Full time—Dr P Anderson and Dr N E Shaw demonstrators in anatomy, Dr K D Neame and Dr F A Jenner, assistant lecturers in physiology, Dr W D Smith, research assistant in medicine

Part time—Dr D A J Tyrrell hon lecturer in medicine, Dr J D S Hammond tutor in medicine for dental students

Royal Medical Benevolent Fund

The annual general meeting of the Fund is to be held on Thursday, July 28, at 5 P M, at 11, Chandos Street, London W 1, with Lord Webb Johnson, the president, in the chair

R A F Appointment

Air Commodore F E Lipscomb has been appointed principal medical officer, Royal Air Force, Home Command, with the acting rank of air vice marshal as from July 1

American Award

A James Picker Foundation grant has been awarded to Dr H A Sissons, morbid anatomist at the Institute of Orthopædics of the University of London, for microradiographic studies of bone structure

Oliver Memorial Fund

The committee of this fund again offer an award of £50 to a British subject for original work or services in connection with blood transfusion Applications should be sent before Aug 31 to the hon treasurer, Mr F W Mills, c/o National Provincial Bank Ltd, Holborn Circus, London, E C 1

National Fund for Poliomyelitis Research

This fund has given £1100 for the purchase of apparatus by the division of human physiology of the National Institute for Medical Research The apparatus will be used at the National Hospital, Queen Square, London, in investigations into cardiorespiratory function in bulbar paralysis conducted by Dr L G C Pugh

The Bone and Tooth Society

This society is holding a public meeting in association with the Ciba Foundation, at 1, Wimpole Street, London, W 1, at 3 P M on Friday, July 15, when some of the proceedings of the Foundation's symposium on *Bone Structure and Metabolism* will be discussed The following members of the symposium will speak Prof A Engstrom (Stockholm), Dr John E Howard (Baltimore), Prof G Fanconi (Zürich), Prof W D Armstrong (Minnesota), and Dr H Lisco (Chicago) Prof R A McCance, F R S, will preside

Prizes for Clinical Research

The following have been awarded prizes in the South West Metropolitan Regional Hospital Board's competition for 1954

Consultants and S.H M O.s—Mr H A. Kidd, St Helier Hospital Dr J F Wallace and Dr Ruth Pillman Aldingbourne Sanatorium Dr D H Bennett Netherne Hospital, Dr J Lomas, Springfield Hospital Dr M M Glatt, Warlingham Park Hospital

Senior registrars registrars and J.H M O.s—Dr E W Ball, South Hants Hospital, Dr J K McKechnie King George V Hospital for Diseases of the Chest, Dr J A Edwards, Knowle and Old Manor Hospitals Mr D A Macfarlane St James' Hospital Balham

Senior house-officers and house-officers—Dr J Kohari, Lambeth Hospital

A similar competition is being held this year and particulars will be sent to group medical committees in the region

Lady Tata Trust

The trustees of this fund announce that they have made the following awards for research on leukæmia and allied diseases, in the year beginning next October

Grants for research expenses—Dr Jorgen Kieler, Copenhagen, Dr Jo Nordmann Paris, Dr Arunachala Sreenivasan Bombay

Scholarships—Dr Flemming Kissmeyer Nielsen and Dr Niels Aksel Stenderup Aarhus Denmark, Dr Jorgen Ringsted and Dr Jorgen Rygaard Copenhagen, Prof H G Teir and Dr C G V Wasastjerna Helsinki

Scholarship and grant for research expenses—Dr Maxime Seligmann Paris

Personal grant—Mr Stanislaw Joseph, Oxford

In addition, a block grant has been made to the Social Medicine Unit, University of Oxford (director, Dr Alice Stewart), for the cost of a pilot inquiry into possible environmental factors in the ætiology of leukæmia in man

Diary of the Week

JUNE 26 TO JULY 2

Monday, 27th

Postgraduate Medical School of London, Ducane Road, W 1
4 P.M Dr R Bing (Alabama) Metabolism of the Heart.

Tuesday, 28th

Institute of Dermatology, St John's Hospital, Lisle Stree W C 2
5 30 P M Dr P D Samman Follicular Keratotic Disorders

Wednesday, 29th

Royal Society of Medicine, 1 Wimpole Street London W 1
4 30 P M *Physical Medicine* Dr Philippe Bauwens Dr W Levitt, Dr Robert Forbes Medicolegal Problems and t Department of Physical Medicine
Institute of Dermatology
5 30 P M Dr Henry Haber Dyskeratoses

Thursday, 30th

Postgraduate Medical School of London
4 P M Dr J F Goodwin Mitral Valve Disease
Royal Society of Medicine
2 30 P M. *Urology* Mr J Cosbie Ross Mr N O K Gibbo Mr David Band Dr A G Hardy Paraplegic Bladder
British Association of Urological Surgeons
9 30 A.M (Royal College of Surgeons of England, Lincoln's In Fields W C 2) Opening of annual meeting
Renal Association
4 30 P.M (41 Portland Place, London W 1) Dr Alexander Le (Boston), Dr Oliver Wrong Volume Control of the Bod Fluids

Friday, 1st

Postgraduate Medical School of London
2 P.M Prof H A Magnus Reticulosarcoma of Bone
4 P M Dr W W Brigden Rheumatic Carditis
Institute of Laryngology and Otology, 330, Gray's Inn Roa W C 1
3 30 P M Mr Wallace Black Congenital Deafness

Appointments

Barclay, David, M B Aberd, D.P H deputy M O H, Aberdeen
Davies, Dewi, M D Lond, M R.C P physician superintenden Ransom Sanatorium Rainworth, Notts, consultant physicia Mansfield chest clinic
Gilliatt, R W, D M Oxfd, M R C P asst physician, Nation Hospital, Queen Square, London
Halliwell Jean M., M B Manc, D OBST, D C H school M Stockport
MacLeod, M. C, M B Glasg, D P H. senior M O and school M Dorset
Manning, Angela, M R C.S asst M O and school M O, Warringto
Patterson Janet B, M B Aberd school M O and asst M O.H Middlesbrough
Rose Clement M D Lond D P M. whole time consultant psych atrist Mapperley Hospital, Nottingham.
Short, Richard, L R C P E D P H area executive M O Nort nos 1 and 2 areas, and M.O H, urban districts of Alnwick an Amble rural districts of Alnwick, Glendale, Rothbury an Norham and Islandshires Northumberland
Swinney, W D M B Aberd, D P.H divisional M O H, Surre (Merton and Morden part of North Eastern Division), M O H Merton and Morden U D C
Watters N M M B Glasg whole time asst ophthalmologis Rotherham Mexborough, and Worksop areas, Sheffield R H B

South Western Regional Hospital Board

Bradfield A M M B N Z registrar in psychiatry, Brist mental hospitals
Edwards, E M. M B Lond, M R C O G, D OBST temporar senior registrar in obstetrics and gynæcology, Bristol clinic area
Hargadon, E J, M B Wales surgical registrar, Cossham Frenchay hospital group Bristol
Roberts, A. G M B B.SC Wales registrar in psychiatry, Moorhaven Hospital, Ivybridge, South Devon
Theobalds, J R. M R C.S medical registrar, Cheltenham General, Eye, and Children's Hospital
Wells A. M, M B Brist D OBST, D C H medical registrar Southmead Hospital, Bristol

Leeds Regional Hospital Board

Calderwood R. W L F R C S asst orthopædic surgeo (S H M O) Pontefract and Castleford group
Hird G F, F R C.S asst orthopædic surgeon (S.H.M.O) Huddersfield group
McCrea P C, M B Belf asst pathologist (S H.M O), Harrogate and Ripon group
March H F, M B Durh, M R.C P, D.M R.D consultant radiologist, York (A) and Tadcaster, and Scarborough, Malton, and Whitby groups
Mather Ida M.B Leeds, D P M asst psychiatrist (S.H M O), Stanley Royd Hospital, Wakefield

Appointed Factory Doctors

Houghton, H J M B Wales Llandrindod Wells Radnorshire.
Lewis, M. P, B.M Oxfd, D OBST Oundle, Northants

INDEX TO VOLUME I, 1955

REFERENCES AND ABBREVIATIONS

Institutions and Corporations with the right to the prefix Royal will be found under that prefix with the exception of Medical Societies which are separately indexed under Societies All Universities are indexed under the word Universities (A) = Annotation (C) = Correspondence (LA) = Leading Article, (ML) = Medicine and the Law, (NI) = New Invention (O) =Obituary, (P) = Parliament and (R) = Review

A Concordance of page numbers and dates of issue will be found on opposite page

A

Abbas, T M. torsion of fallopian tube 128
Abbatt, J D ankylosing spondylitis 1283
Abbott J D Sonne dysentery 16
Abbott M., Atlas of Congenital Cardiac Disease (R) 138
A.B.C of Food and Child Feeding (Clark) 1226
Abdomen, see Intestines Omentum
Abercrombie G F Emergency Bed Service (C) 201
Aberdeen research on obstetrics in 1335
Abraham H C organic brain disease (C) 513
Abscess hepatic secondary to duodenal ulcer (Antia and Markor) 649
Abundance and want (Pullar-Strecker) (C) 1072
Accidents—accident prone (LA) 547; Sutton Coldfield railway accident 298 (Gleave) (C) 569 (Scott) (C) 621 to eyes 91
Acetazoleamide—(LA) 706 (Simpson) (C) 870; in acute respiratory acidosis (Wibhart and Isaacs) 995 in glaucoma 931
Achalasia of cardia in adolescents presenting with respiratory symptoms (Davies and Roberts) 840 (Gibson) (C) 969
Acheson R M growth in first five years 691
Acidosis, see Acetazoleamide
Actinomycosis treated with hydroxystilbamidine (Hancock) (C) 1123
Adams, C. W M. pituitary gland, 651
Addiction to drugs—I was a Drug Addict (Street and Loth) (R) 1006 methylpentynol (Glatt) (C) 308, minor addictions 1264, not cruelty (ML) 911 pethidine (ML) 97 see also Heroin
Adenosine and heart (A) 1113
Adenosine triphosphate in paroxysmal tachycardia (Somló) (C) 1125
Adenotriphosphatase in herpes zoster (Hrous) (C) 616
Adrenal, see Suprarenal glands
Adrenalectomy, see Suprarenal glands
Adrenaline effect of, on adrenocortical secretion (Hunter Bayliss and Steinbeck) 884
Adrenocortical see Suprarenal glands
Adrenogenital syndrome treated with cortisone and oestrogen (Armstrong) 1051
Adrenolytic effect of phentolamine and chlorpromazine (Knox and Sleeur) 790
Adriani, J Nerve Blocks (R) 800
Advances in Ophthalmology (R) 84
Advances in Virus Research (Smith and Lauffer) (R) 1106
Aerosol therapy in chronic bronchitis due to H influenzae (Knox Elmes and Fletcher) 120
Africa—medical care in South African township (Susser Cormack, Stein and Hathorn) 612, peptic ulcer in Southern Nigeria (Smith) (C) 50 (Rose) 107 (Konstam) (C) 870
Africans, mongolism in (Luder and Musoke) (C) 62
Agammaglobulinaemia (Weiner) (C) 108 (Zoutendyk, Anderson Kahn and Stein) (C) 1075
Aged—(P) 181; Ageing Men in Labour Force (Clark) 262 Geisteskraft und Geistesstörung im Alter (Kielholz Stoll, Weber Ittel, and Wyrsch) (R) 1058 Geriatric Medicine (Stieglitz) (R) 180; in homes pocket money and charges for 118 in their homes 808, in welfare homes, 1335 patients almoners and (LA) 600 Warren (C) 673 patients in Edinburgh needs of (P) 814 sick care of (P) 301 work of geriatric unit (Gibson) 960
Agene (A) 33 (P) 53
Agerholm, M. quarantine in poliomyelitis (C) 1327
Agglutinins see Blood
Aidin, R pulmonary embolism (C) 101
Air—in infant's alimentary tract (A) 400 pollution (P) 301 radioactivity of in London (P) 814 transport of tuberculous (A) 341
Aircraft disasters injuries in Comet (Armstrong Fryer Stewart and Whittingham) 1135
Air-embolism—associated with ruptured uterus (Scrimgeour and Cairick) 485 (Snell) (C) 615 (Birch) (C) 720 during artificial pneumoperitoneum (ML) 799
Aksoy M., sickle-cell trait, 589
Al Aki F M. Surgical Technigrams (R) 288
Alcoholics, treatment centre for in mental hospital (Glatt) 1318
Alcoholism (Pullar-Strecker) (C) 1072
Aldis G, Hospital Planning Requirements (R) 598
Aldosterone—increased excretion of immediately after operation (Llaurado) 1295 primary aldosteronism 1167
Alevaire (A) 601
Alexander H L. Reactions with Drug Therapy (R) 1005
Alexander J G sterilisation of syringes (C) 1228
Alexander, J O D dermatitis herpetiformis, 1201
Alexander P—Fundamentals of Radiobiology (R) 902 Radiobiology Symposium, 1954 (R) 845
Alexander the Great and his Time (Savill) (R) 1006
Alford A. F mental health 1233
Alkaptonuria (Harris) (C) 120
Allan, T Scalpel Sword 57
Allen F V Peripheral Vascular Diseases (R) 1301
Allen & Hanburys Ltd—Through a City Archway (Chapman Huston and Cripps) 573
Allergy—hormone balance in, 1004 hydrocortisone in treatment of allergic conjunctivitis and allergic rhinitis (Foulds, Greaves, Herxheimer and Kingdom) 234
Allison A C, vitamin K (C) 669
Allison, P R, measurement of pressure in left auricle pulmonary artery and aorta 9
Allowances for children (P) 350
Almoners and aged patients (LA) 600 (Warren) (C) 673
Aluminium water pipes and utensils 884
Ambrose G—enuresis (C) 456 epilepsy (C) 972
Ambulance patient's death after journey in (ML) 96
America—malaria in (A) 292 Sindrome Policarencial Infantil (Kwashiorkor) and its Prevention in Central America 573 see also U.S.A
American College of Surgeons 311
Amines aromatic hypersensitivity to (Barnes and Barnes) (C) 455 (Hill) (C) 617
Aminosugars—Biochemistry of Aminosugars (Kent and Whitehouse) (R) 1057
Ammonia see Nitrogen
Amoebiasis, see Dysentery
Amphetamine—Amphetamine in Clinical Medicine (Bett Howells and Macdonald) (R) 909, in treatment of depression (A) 1065 (Skottowe) (C) 1129 (Hindolf) (C) 1178
Ampin automatic ampoule injector 57
Amputations—Amputations (Gillis) (R) 186 outlook for amputees (A) 89; Syme's amputation (Wellish) (C) 102, transmetatarsal amputation in arterial insufficiency of lower limb (Norman) 919
Amyl acetate in resuscitation of newborn (A) 601
Amylase level in serum in mumps meningo-encephalitis (Wallman and Vidor) 1105
Anaemia—aplastic following mepacrine treatment of lupus erythematosus (Paton, Riddell, and Strong) 281 cobalt and (LA) 666 (LA) 131 due to pure red cell aplasia treated successfully with cobalt (Fountain and Dales) 541 (Chalmers) (C) 72 haemolytic acquired, corticotrophin and splenectomy in (Barrie and Blackburn) (C) 205 in general practice 82 iron-deficiency in pregnancy (Gatenby and Lillie) 740 (Redman) (C) 971 megaloblastic due to spontaneous ileocolic fistula associated with subacute combined degeneration of spinal cord (Wilkinson) 71 nutrition and (LA) 666
Anaesthesia—anaesthetist looks at burnt child (Shannon) 111 (Davison) (C) 169, effect of on fibrillation (Barnard) (C) 824 (Ballantine Jackson and Wells) (Hewer) (C) 921 in obstetrics (A) 968 labour ward bed for safer (Gibberd) (NI) 901 Nerve Blocks (Adriani) (R) 800, orotracheal connection with minimal resistance (Bullough) (NI) 236 571 Practice of Local Anaesthesia (Bankoff) (R) 134; Stellate Ganglion Block (Moore) (R) 800 see also Cyclopropane
Analgesia—Analgésie obstétricale (Jamain and Giraud) (R) 598 continuous conduction in eclampsia (Bryce-Smith and Williams) 1241 new analgesic (A) 317 phenylbutazone as analgesic (Crowe) (C) 1076
Anatomy—Maxillofacial Anatomy (Shapiro) (R) 387; Prefrontal Leucotomy and Related Operations (Meyer and Beck) (R) 132 Röntgenanatomische Grundlagen der Lungenuntersuchung (Kovats and Zsebök) (R) 936
Anderson A W sanatoria (C) 972
Anderson, C O agammaglobulinaemia (C) 1075
Andrade, C. R amoebic dysentery (C) 977 (C) 1221
Andrejevic M. pyloric stenosis (C) 400
Andrews, G C. Diseases of Skin (R) 593
Aneurysms—dissecting aneurysm of aorta (Thomson and Mason) 452 (FitzGerald and Watson William) (C) 616 non pulsatile aortic aneurysm (Breckenridge) (C) 622, of circle of Willis (A) 139
Angel, R. W corporal punishment (C) 1125
Angiitis, see Arteries
Angina see Heart
Angiocardiography in chest disease (A) 1316
Anning S T Leg Ulcers (R) 138
Anopheles gambiae—Biology of Anopheles gambiae (Holstein) (R) 131
Anophthalmos see Eyes
Ansolysen see Pentolinium Tartrate
Antenatal and Postnatal Care (Browne and Browne) (R) 1006
Anthrax and bone meal fertilisers (Jamieson and Green) 560
Antia F P hepatic abscess, 649
Antibiotics—(Cohen) (C) 46 abuse of (LA) 1059; resistance of meningococci to (A) 90, see also Dysentery
Antibodies incomplete papain treated red cells in detection of (Goldsmith) 70

oagulants in myocardial infarction 32
tamines as hypnotics (A) 958, rs) (C) 1331
retics too many? (Bronsdon) (C) 57 (Sherwood) (C) 306, (O'Connor) (Bronsdon) (C) 406
Anuria—in aspirin poisoning (Miller) 596, prolonged, treated by infusion into vena cava (Chalmers and Fawns) 79
Any Questions? (R) 186
Aorta—bronchoscopic approach for measuring pressure in (Allison and Linden) 9, *see also* Aneurysms
Aortic stenosis, *see* Heart
Aphonia (Carter) 908
Apoferritin (A) 552
Appendicitis—and fear (Ribeiro) (C) 621, diagnosis of (Kerr) 736, (Keizer) (C) 972, (Horwitz) (C) 1027, (Kerr) (C) 1279
Appetite, perverted (Muir) (C) 306
Arachnodactyly (A) 1062
Archivos de Neurobiologia, 110
Argentaffinoma—as endocrine tumour (Page, Corcoran Udenfriend, Sjoerdsma, and Weissbach) (C) 198, (correction) 406, *malignant, with cyanosis and pulmonary* stenosis (Jenkins and Butcher) 331
Arginine deficiency and cancer (Miller) (C) 970
Armstrong C N, adrenogenital syndrome, 1051
Armstrong J A, Comet aircraft disasters, 1135
Armstrong, T G, amœbic dysentery (C) 1224
Army, *see* SERVICES
Arnaud J D, appointments in W Indies (C) 822
Arnold R shoe design (C) 1078
Aron K W psychiatric day hospital (C) 724
Arrhenoblastoma, ovarian, causing virilism (Evans and Jones) 436
Arsenic in food, 610
Art—holes knobs and wires (Turner) 763 (Atkin) (C) 821, Insanity, Art and Culture (Reitman) (R) 752, Meaning and Symbol (Digby) 926, *see also* Exhibition
Arteries—angiocardiography in chest disease (A) 1315 anterior choroidal artery (LA) 1100, arterial insufficiency of lower limb, transmetatarsal amputation in (Norman) 949, arteriography of digital, in Raynaud's disease (Lynn, Steiner and Van Wyk) 471, broncho*scopic approach for measuring pressure* in pulmonary artery (Allison and Linden) 9 cerebral, disease of (A) 139 (Blumenthal and Handler) (C) 615, femoral artery blood transfusion into (Neve) 746 hypersensitivity angiitis (Edge, Fazlullah, and Ward) 1153, *intra*-arterial blood transfusion in diabetic coma (Kalbag and Naish) 1152 palmar blood supply (A) 603 single stage method of freeze-drying, for grafting (Hewett, Zinnemann Oldfield, Shucksmith, and Dexter) 888, *see also* Aneurysms, Aorta, Atheroma, Atherosclerosis Coronary, Periarteritis nodosa, Raynaud s phenomenon
Arthritis *see* Osteo arthritis, Rheumatoid arthritis
Arthrodesis, compression clamp for, of first metatarso phalangeal joint (Hulbert) (NI) 597
Arthroplasty in late treatment of congenital dislocation of hip, 1309
Artificial Respiration (Garland) (R) 545, 1323
Asbestosis lung cancer in (A) 1163, (Knox) (C) 1275
Ascariasis treated with piperazine derivatives (Dunn) 592
Ascites (LA) 755, 850, complicated by hydrothorax (Emerson and Davies) 487
Ashby D W, pentolinium tartrate, 224
Ashby, M, tuberculous meningitis, 65
Asher R talk, tact and treatment 758
Aspinall R S (O) 108
Aspiration trocar and cannula (Robson) (NI) 1300
Aspirin—fate of (A) 550 poisoning, suppression of urine in (Miller) 596
Assinder, E W, venereology and dermatology (C) 818
Association of British Pharmaceutical Industry 927
Asthma—bronchial, treated with hydrocortisone (Foulds Greaves, Herxheimer, and Kingdom) 234, skin tests in (A) 294
Astley, R., thrush œsophagitis 991
Atheroma of cerebral arteries (A) 139
Atherosclerosis—diet and (Walker) (C) 565, effects of on coronary circulation (Duguid and Robertson) 525
Atkin I.—art (C) 821, mental health (C) 307
Atlas of Congenital Cardiac Disease (Abbott) (R) 438
Atlas of Operations for Trauma (Russe) (R) 1057
'Atlas' syringe, 519
Atom bombs, *see* Irradiation
Aureomycin and vaccine lymph (A) 498 (Francis) (C) 872
Auricle, *see* Heart
Auxiliary Heart (Wasson) (R) 653
Avery O T (O) 463 571
Aviation medicine textbook of adopted for use of medical officers of Royal Air Force (P) 412

B

Baar, H S, tetany and potassium deficiency (C) 459
Babcock's Principles and Practice of Surgery (Jonas) (R) 387
Babies—air in alimentary tract of (A) 496, Antenatal and Postnatal Care (Browne and Browne) (R) 1006 artificial feeding of (A) 443, baby's death after fumigation of perambulator (ML) 912, Développement psycho moteur du premier âge (*Koupernik*) (R) 438, *Diseases of* Infancy and Childhood (Sheldon) (R) 1108, disorders of, 56, *Escherichia coli* in diarrhœa of (Ogawa and Ogawa) (C) 671, experiments on (P) 452, (P) 453, first ten minutes (A) 757, height, weight, and skeletal maturity in first five years of life (Acheson, Kemp, and Parfit) 691, hyaline membrane in lungs of newborn (Lynch and Mellor) 1002, hypothermia in newborn (Mann) (C) 613, (Smallpeice) (Jones) (C) 679 (Braithwaite) (Williamson) (Polani) (C) 773 Infant Feeding and Feeding Difficulties (Evans and MacKeith) (R) 288, Infantile Cerebral Palsy (film) 1117, instinct and nursing couple (Gunther) 575, interstitial emphysema in, 951 intestinal obstruction in newborn (A) 292, lymphocytic choriomeningitis in newborn (Komrower Williams, and Stones) 697, newborn, identification of, 211, (P) 507, Pædiatrics for Practitioner (Gaisford and Lightwood) (R) 704, physical environment of (A) 1211, premature, hypothermia in (A) 498, resuscitation of newborn (A) 601, staphylococcal infection in newborn, treated with erythromycin (Forfar Maccabe, Balf, Wright, and Gould) 584 (Court, Green, Hutchison, and Neligan) (C) 969, (Forfar, *Maccabe, Balf, Wright, and Gould) (C)* 1071, (Hay) (C) 1127, (Court, Green, Hutchison, and Neligan) (C) 1226, thrombocytopenia due to platelet agglutinins in newborn (Vandenbroucke and Verstraete) 593 vitamin K dangerous *to (Allison) (C) 669 (Moore and Sharman)* (Laurance) (C) 819, *see also* Congenital defects, Paralysis, Social and biological factors of infant mortality
Bacq Z M—Fundamentals of Radiobiology (R) 902, Radiobiology Symposium, 1954 (R) 545
Bacteria—anaerobic cocci (A) 293, Biochemical Determinants of Microbial Diseases (Dubos) (R) 704, chemically identifiable residues of in lung lesions (Consden and Glynn) 943, Clinical Bacteriology (Stokes) (R) 653, contamination of London's water-supply by, 863 flagella of (A) 700, genetics of, 145, in industry, 261, pleuropneumonia-like organisms (Stokes) 270, *see also Clostridium welchii, Escherichia coli,* Hæmophilus, Meningococci, Staphylococci Streptococci
Badenoch, A W cystoscopy diagram stamp (C) 626
Baensch, W E, Roentgen Diagnostics (R) 186
Bailey, D median nerve palsy 530
Bailey, H, Physical Signs in Clinical Surgery (R) 388
Baker, D Cardiac Symptoms in Neuroses (R) 1206
Baker, G P, hospital staffs (C) 563
Baker H B, cancer (C) 1075
Balf C L, staphylococcal infection 584, (C) 1071
Balint M doctor, patient, and illness, 683
Ball K. lung cancer (C) 155
Ballantine, R I W anæsthesia and heart (C) 921
Ballard, J F (O) 1132
Banerji R thrombophlebitis (C) 514
Bankoff G, Practice of Local Anæsthesia (R) 134
Banks, A. L—cancer (C) 515, Development of Tropical and Subtropical Countries (R) 654
Bantu, South African, tuberculin and lepromin sensitivity in (Kuper) 996
Barber H W (O) 207
Barbiturate—addiction to 1264, antagonist (Harris) 181 (correction) 262 (Montuschi and Wickenden) (C) 622 (McElligott) (C) 820, (Shaw) (C) 969, (Wright) (C) 1073, (Shaw and McCallum) (C) 1225, (Wright) (C) 1329, poisoning (Kellock) (C) 308
Barer, R., Lecture Notes on Use of Microscope (R) 438
Barker, N W, Peripheral Vascular Diseases (R) 1310
Barlow, J cholangiography, 13
Barlow W, Isobel Cripps Centre 156, (C) 257, (C) 358
Barnard, J, anæsthesia and fibrillation (C) 824
Barnes, J, and Barnes, E J, hypersensitivity to primary aromatic amines (C) 455
Barnett, A J, Raynaud's phenomenon (C) 1328
Barnett Sir G, report of, for 1953, 94
Barrie, W J G, *hæmolytic anæmia (C)* 205
Barry, D T (O) 925
Barry, M. sarcoidosis, 483
Basal metabolic rate during sleep (Fraser and Nordin) 532
Bassir, O, laboratory inaccuracy (C) 677 (C) 821
Baths, cold (Vincent) (C) 516, (Dickson) (C) 564
Battery casings used as fuel, poisoning by (Gillet) 1118
Bavin, E M isoniazid derivative (C) 303
Bayliss, R. I S—adrenocortical secretion, 884, 17 hydroxycorticosteroids, 62
Bayly, M. B, 'Hydergine' (C) 1329
Bayne, J R. D, chronic patients, 1317
'Baytenal' (Nobes) 707
B C G vaccination (Heaf) 315, (Webster) (C) 511, (Loxton) (C) 619, (Doig) (C) 724, (A) 756, (Heaf) (C) 771, (Briggs) (Friedmann) (C) 869
Beales, P H, laryngeal cancer (C) 257
Beare, J M., molluscum sebaceum, 182
Beattie, P H optic atrophy, 650
Beaven, C, philosophy and therapeutics (C) 200
Beaven, D W, hexamethonium 371
Beaver Committee, main recommendations of (P) 301
Beck, A, torulosis, 535
Beck, E—leucotomy 23, Prefrontal Leucotomy and Related Operations (R) 132
Beckett, A G, thrombocytopenic purpura, 1053
Beddard, F D, tuberculin testing (C) 49
Bedford, P D, vitamin B_{12} (C) 1129
Beds—dangerous cots (A) 1261, (Herzog) (Kisch) (C) 1332 for paying patients in hospitals (P) 351, labour-ward for safer anæsthesia (Gibberd) (NI) 901 *see also* Emergency Bed Service
Bedson, S P Virus and Rickettsial *Diseases (R) 1256*
Bedwetting (Holman) (R) 133, (LA) 391 (Symonds) (C) 455 (Ambrose) (C) 456, (Smith) (C) 511, (Poulton) (C) 616, (Symonds) (Nash) (C) 676, (Kahn) (C) 774, (Hodge) (C) 807 (Lowenfeld) (C) 1020, (Cosgrave) (C) 1228
Bee stings, median nerve palsy following (Birch) (C) 619
'Beetle Resin' (Maudsley) 847

BEFORE OUR TIME—James Parkinson (Morris) 761—Medical mission 1855 (Laws) 147

Behçet's syndrome (Phillips and Scott) 366, (Church and Sneddon) (Shubert) (C) 511 (Freedman) (Whitwell) (C) 569, (Pappworth) (C) 820
Beit fellowships for medical research, 1183
Belgium, smallpox in, 410
Bellwood K B (O) 977
Belyavin, G influenza virus, 698
Bender A E, lung cancer (C) 354
Bendick A J, Diagnostic Advances in *Gastrointestinal Roentgenology (R)* 1006
Beneventi F A Retropubic Prostatectomy (R) 1057, (correction) 1134
Bentley, F J, sanatoria (C) 99
Bentley, G A, pituitary gland, 386, (C) 775
Berenbaum, M C, myoglobinuria, 892
Berens H A., Chinese medicine (C) 1220
Bett, W R., Amphetamine in Clinical Medicine (R) 902
Beven, G sanatoria (C) 614
Bickerstaff, E R., tumours of glomus jugulare (C) 255
Bickford J A R, epidemic vertigo (C) 305
Bidstrup, P L, mercury (C) 672
Bignall, J R bronchial cancer 786
Bile, pH and buffering power of (Crawford and Brooke) 1096
Bile-duct, *see* Cholangiography
Billroth I Gastric Resection (Moore and *Harkins) (R) 30*
Biochemistry—Biochemical Determinants of Microbial Diseases (Dubos) (R) 704, biochemical disturbance in hepatic coma (LA) 1258, Biochemistry of Amino-

sugars (Kent and Whitehouse) (R) 1057 Biochemistry of Semen (Mann) (R) 84, Chemistry of Lipids of Biochemical Significance (Lovern) (R) 387 Physiology and Biochemistry of Skin (Rothman) (R) 133
Biology—Biology of *Anopheles gambiae* (Holstein) (R) 134 Chemistry and Biology of Pteridines (Wolstenholme and Cameron) (R) 654
Birch, C. A.—air-embolism (C) 790; median nerve palsy after bee-stings (C) 619, myoglobinuria 892
Bird C. A. K. Notes on Transfusion (C) 256
Birth-control in Colonies (P) 51
Black, D. A. K. fate of intravenous potassium, 1097
Blackburn, E. K.—cancer (C) 566 hæmolytic anæmia (C) 205
Blacklock, D. B. death of, 1262 (O) 1332
Bladder see Urinary bladder
Blaikley R. M. breast cancer (C) 817
Blake J. C. meningitis 383
Bland-Sutton Sir John (A) 907
Blankets—electric British standard 1184; electric burns from (Davis) (C) 710 (Maddison) (C) 817 (Grisley) (C) 973 (Strutt) (C) 1225 sterilisation of with cetyl trimethylammonium bromide (Blowers and Wallace) 1250 (Marsh) (C) 1331
Blind, see Eyes
Blockey N. J. sandal (NI) 286
Blood—assessment of blood-loss in civilian trauma (Clarke, Topley, and Flear) 679 erythrocyte-sedimentation tubes British standard 211 erythrocytes labelled with isotopes in testing for incompatibility in vivo (Mollison and Cutbush) 1290, estimation of oxygen in (Handforth) 1252 Hæmatological Technique (Darmady and Davenport) (R) 335, hæmoglobinuria, paroxysmal nocturnal (Douglas and Eaton) 946, levels of pyruvic acid and of α-ketoglutaric acid in health and in diabetes (Smith and Taylor) 27, loss estimation of (LA) 1003, (de Wardener) (C) 1125, Modern Trends in Blood Diseases (Wilkinson) (R) 1107 palmar blood-supply (A) 603, papain treated red cells in detection of incomplete antibodies (Goldsmith) 70 red-cell aplasia, pure treated successfully with cobalt (Fountain and Dales) 511, serum-amylase levels in mumps meningo-encephalitis (Wallmann and Vidor) 1105 serum proteins electrophoresis of (A) 604 (Owen) (C) 868 (Camden) (C) 1026 (Miltényi) (C) 1181 (Christiansen) (C) 1227 serum tests for syphilis (Wilkinson) (C) 100 sickle-cell trait in S Turkey (Aksoy) 559 (Lehmann) (C) 673 tests and motoring offences (P) 967 thrombocytopenia due to platelet agglutinins in newborn (Vandenbroucke and Verstraete) 593 see also Agammaglobulinæmia Anæmia Hæmophilia, Leukæmia Nitrogen Purpura, Uræmia
Blood-flow—Digital Circulation (Mendlowitz) (R) 1057 splenic (LA) 338; see also Uterus
Blood-pressure—bronchoscopic approach for measuring in left auricle pulmonary artery and aorta (Allison and Linden) 9
Blood transfusion—exchange in sodium nitrite poisoning (Kirby) 594 hæmolytic reactions to (Discombe) (C) 99 (Stephen) (C) 156 incompatibility testing for (Mollison and Cutbush) 1290 incompatible (ML) 1271 into femoral artery (Novo) 746 intra-arterial in diabetic coma (Kalbag and Naish) 1162; massive, through cephalic vein (Dolton) 1032 Notes on Transfusion (C) 205, (Bird) (C) 256 of battle casualties (A) 311 pilot tube for blood bottle (Campbell) (NI) 1038, pump (Landau) (C) 50 (Keating) (C) 151
Blood-vessels—cutaneous vasodilatation during fainting (Snell, Cranston and Gerbrandy) 693 fibrinous vasculosis 851 Peripheral Vascular Diseases (Allen Barker and Hines) (R) 1310 vascular phenomena in infection 1004; see also Arteries, Embolism, Veins
Blowers, R. sterilisation of blankets, 1250
Blumenthal, H. T. cerebral arterial disease (C) 615
B.M.R. during sleep (Fraser and Nordin) 532
Boardman R. H. chlorpromazine 1144
Boards of governors of teaching hospitals, 1321
Bodies, number of bequests of (P) 453
Body-build and temperament (LA) 291
Bolton Carter J. F. median nerve palsy 530
Bone-marrow—infusions into (A) 604 stimulation of erythroblastic mitoses in by pituitary gland (Marinone and Corso) (C) 373
Bone-meal and anthrax (Jamieson and Green) 560
Bones—lungs and joints (A) 340 (Fliman) (C) 403 Maladies des os et des articulations (de Sèze and Ryckewaert) (R) 438 osteosclerosis due to chronic infection or to neoplastic infiltration (Weber) 386, skeletal maturity in first five years of life (Acheson Kemp and Parfit) 601
Bonham Carter R. E. continuous murmurs 27
Bonnell J. A. mercury (C) 672
Books—Scientific Books Libraries, and Collectors (Thornton and Tully) (R) 30
Bourdillon R. B. nuclear explosions (C) 866
Bourg R. Diagnostic cytologique du cancer génital chez la femme (R) 800
Bourne G. H.—International Review of Cytology (R) 387 prostatic cancer 481
Bourne I. H. J. protecting motorist (C) [illegible]
Bourne J. G. cyclopropane and sparks, 70
Bourne W. A. abdominal operations (C) 51
Bowels see Intestines
Bower, A. G. Diagnosis and Treatment of Acute Phase of Poliomyelitis (R) 1255
Boxing—eye injuries in 1335 head injuries in (A) 1114
Boycott J. A. vipers (C) 306
Boys, L. cancer (C) 1274
Braatoy T. Fundamentals of Psychoanalytic Technique (R) 336
Brackenridge G. R. aortic aneurysm (C) 622
Bradley J. E. S., radioactive sodium, 419
Bradley S. E. Renal Function (R) 288
Bradshaw, F. L. cancer of respiratory tract, 861
Brafield F. adrenal cortical function (C) 468
Brailsford, J. F.—post pregnancy osteoporosis (C) 513 sanatoria (C) 98
Brain—arteries of, diseases of (A) 139 (Blumenthal and Handler) (C) 615 Brain Mechanisms and Consciousness (Delafresnaye) (R) 600; cerebellar degeneration (A) 444 cerebral thrombosis in young adults (A) 1065 Cerebrospinal Fluid (Lups and Haan) (R) 1206, cerebrospinal fluid in carcinomatosis of meninges (Murphy) 231, (Shafar) (C) 408 encephalopathy Wernicke's (A) 91 experiments on (Jefferson) 59 functional symptoms of organic disease of (Pritchard) 863 (Abraham) (C) 513 intraventricular administration of drugs 900 methyl mercury poisoning (A) 35, peptic ulcer and (LA) 495 Rôle of Mental Function in Physical Activity (film) 146 Spino-cerebellar Degenerations (Greenfield) (R) 30 treatment of frontal lobes with ultrasonic waves (A) 38 *see also* Choriomeningitis Electroencephalography, Epilepsy Leucotomy Meningitis, Paralysis
Braithwaite F. modified Humby knife (NI) 1004
Braithwaite, J. V. hypothermia (C) 773
Bramwell, C. rheumatic valvular disease 213
Brandes D. prostatic cancer 481
Brande H., maize and pellagra 898
Brearley H. pilonidal sinus (C) 923
Breast cancer—clinical staging of (Harmer) (C) 670, (Blaikley) (C) 817, (Harmer) (C) 1128 fibro-adenosis and (A) 35 (Saner) (C) 720, non progressive (McKinnon) (C) 1028 (C) 1124 pituitary radon implant for (Forrest and Peebles Brown) 1054
Breast feeding (Gunther) 676 (Jelliffe) (C) 1024
Breathing exercises action of, in pulmonary emphysema (Campbell and Friend) 325
Brehme T.—poliomyelitis (C) 156 retrolental fibroplasia (C) 671
Brennan, J. B. plastic splints, 841
Briggs, H., tuberculosis, 263
Briggs, I. L. B.C.G. (C) 809
British Association of Physical Medicine 908
British Journal of Anæsthesia 212
British Journal of Hæmatology (A) 498
British Medical Association, 928, 1218
British Medical Bulletin 463 1230
British Pharmacopœia 1117
British Practice in Radiotherapy (Carling Windeyer and Smithers) (R) 752
British Society for Research on Ageing, 730
British Standards Institution standard for—electrically heated blankets, 1184 erythrocyte-sedimentation tubes, 211 flexible lead-rubber gloves, 980 gas cylinder trolleys 1032 terms used in radiology 1184
British Student Tuberculosis Foundation (Malleson) (C) 304
British Surgical Practice Surgical Progress 1954 (Carling and Ross) (R) 288
British Tuberculosis Association 110
Brockington C. F. housing 244
Brockway, A. Operative Orthopedic Clinics (R) 1236
Brodhage H. pyridyl-oxdiazolones in tuberculosis (C) 570
Bromberg W. Man Above Humanity (R) 492
Bronchi—bronchial asthma treated with hydrocortisone (Foulds, Greaves Herxheimer and Kingdom) 234 bronchitis treated with inhalation of trypsin (Simpson) (C) 48, bronchography (Pygott) (Rackow) (C) 47 bronchoscopic approach for measuring pressure in left auricle pulmonary artery and aorta (Allison and Linden) 9 cancer of (Bignall) 786 cancer of associated with sensory neuropathy (Smith and Whitfield) 262 cancer of cell type in (LA) 954, cancer of incidence of, in relation to that of laryngeal cancer (Maxwell) 193 (Beales) (C) [illegible]57 (Maxwell) (C) 506, chronic due to *H. influenzæ*, aerosol therapy in (Knox Elmes and Fletcher) 120 new right endobronchial tube (Gordon and Green) (NI) 185 tracheobronchitis, postoperative membranous (Dark and Jewsbury) 430 (Colto and Flora) (C) 873
Bronsdon, N. P. antipyretics (C) [illegible]57 (C) 406
Brooke B. N.—bile 1096, carcinomatous obstruction of colon 945
Brooke C. O. S. B. health centres 93
Brotherston J. H. F., appointment 1183
Brous M. herpes zoster (C) 616
Brown A. E., appointment 628
Brown, C. R. (O) 158
Brown, E. V. (O) 571
Brown H. Challenge of Man's Future (R) 952
Brown, J. B., œstrogens 390
Browne, F. J. Antenatal and Postnatal Care (R) 1006
Browne J. C. M.—Antenatal and Postnatal Care (R) 1006, 17 hydroxycorticosteroids, 62 radioactive sodium, 419
Browne R. C. lead poisoning (C) 775
Brucellose als Anthropo-Zoonose (Löffler Moroni and Frei) (R) 438
Bryce Smith, R. eclampsia, 1241
Buchan J. F. psoriasis spondylitica (C) 1028
Buckley, C. W. death of 1164 (O) 1228
Budget (A) 855, and social services (P) 916
Bdel H. W., Geisteskraft und Geistesstörung im Alter (R) 1068
Bull G. M., uræmias, 731 777
Bullen, J. J. *Clostridium welchii*, 384
Bullough J.—modified Magill's attachment to Boyle's apparatus (NI) 1309; orotracheal connection (NI) 236 674
Burnet J. cancer research (C) 1078
Burns—anæsthetist looks at burnt child (Shannon) 111 (Davison) (C) 199; from electric blanket (Davis) (C) 719 (Maddison) (C) 817 (Grisley) (C) 973 (Strutt) (C) 1225; hyperglycæmia after (Sevitt) (C) 566 (Butterfield) (C) 723; hypoglycæmic effect of dimercaprol in burnt patients (*Butterfield*) 489 (*Rios Mozo*) (C) 973
Burridge W. (O) 977
Burrowes W. L. epidemic vertigo (C) 408
Busson A., Maladies de l'intestin et du péritoine (R) 902
Butcher, P. J. A. argentaffinoma, 331
Butler E. B. *dysmenorrhœa*, 844
Butterfield W. J. H.—dimercaprol, 489; hyperglycæmia after burns (C) 723
Butterflies, irradiated 1183
By any other name (LA) 1257 (Ward) (O) 1333
Byssinosis benefit, 979

C

Cadmium poisoning (P) 453 (P) 806 1019
Cæsium 137 1323
Calcium—deposits in hand (A) 659, disodium (LA) 751 versenate in lead poisoning (Giles, Moore and Still) 183 (Browne) (C) 775 *see also* Uræmia
Caldwell R. S. sanatoria (C) 870
Caley J. I. yellow phosphorus poisoning 539
Callewaert H., Graphologie et physiologie de l'écriture (R) 1310
Calliper light spring (Nickels) 56
Calories and cricket (Fletcher) 1165
Cameron D., mental health and public health (C) 250 (C) 565
Cameron M. P.—Chemistry and Biology of Pteridines (R) 654; Human Adrenal Cortex (R) 1108 Leukæmia Research (R) 30
Campbell, E. J. M. pulmonary emphysema, 325
Campbell J. S. pilot tube for blood bottle (NI) 1038
Cancer—arginine deficiency and (Miller) (C) 970 bronchial (Bignall) 786; bronchial, associated with sensory neuropathy (Smith and Whitfield) 262

bronchial cell type in (LA) 954 bronchial incidence of, in relation to that of laryngeal cancer (Maxwell) 193 (Beales) (C) 257, (Maxwell) (C) 306, cerebrospinal fluid in carcinomatosis of meninges (Murphy) 231 (Shafar) (C) 408 clinical staging of (Harmer) (C) 670, (Blaikley) (C) 817, (Harmer) (C) 1128, clonal ageing and (Platt) (C) 867 clues (A) 392, (Banks) (C) 515, (Nash) (C) 567, cytotoxic agents in (LA) 440, (Blackburn and King) (C) 566, Diagnostic cytologique du cancer génital chez la femme (Bourg, Gompel and Pundel) (R) 800, epithelioma cuniculatum (A) 192, fear of (Zelmanowits) (C) 1126; gastric and peptic ulcer (A) 1161, high pressure oxygen and radiotherapy of (Churchill Davidson, Sanger, and Thomlinson) 1091 hormones and, 490, laryngeal incidence of, in relation to that of bronchial cancer (Maxwell) 193 (Beales) (C) 257, (Maxwell) (C) 306, laryngeal, treatment of (A) 1313, mammary, and fibro adenosis (A) 35, (Saner) (C) 720, mammary, non progressive (McKinnon) (C) 1028, (C) 1124 mammary pituitary radon implant for (Forrest and Peebles Brown) 1054, of respiratory tract (Bradshaw) 861, pain of (Jefferson) 59 palliation of (A) 190, prostatic, and stilbœstrol phosphatase (Brandes and Bourne) 481, psychological disease (Donaldson) 959 (Torrie) (Baker) (Grant) (C) 1075, (Donaldson) (Clapham and Sclare) (C) 1177, (Boys) (C) 1224, pulmonary (Stross) (Mc Clean) (C) 53, (Ball) (C) 155 pulmonary, hardened fats and (Yudkin) (C) 46, (Nyrop) (C) 253 (Bender) (C) 354, (Nyrop) (C) 872, (Yudkin) (C) 1025, (Nyrop) (C) 1178 pulmonary, in asbestosis (A) 1163, (Knox) (C) 1275, pulmonary, in hæmatite miners, 950, pulmonary, mortality of (P) 966, pulmonary, tobacco smoking and (A) 392, (Mims) (Gould) (C) 1180, (Doll and Hill) (C) 1278 relief of pain in incurable (Maher) 18 (Maher) (C) 512, research (Burnet) (C) 1078, (Olbert) (C) 1328 sex of cells of (Tavares) 948 short-wave treatment of 573 simplified operative routine for obstruction of colon by (Brooke) 945, *see also* Argentaffinoma
Capital punishment (ML) 96, (P) 410, (Hinden) (C) 455
Caravan sites, 924, (Hunter) (C) 1128
Carbimazole in thyrotoxicosis (Kirkeby and Remcke) 374
Carbonic anhydrase, diuresis due to inhibition of (LA) 706, (Simpson) (C) 920 (Maren) (C) 1225
Carbon monoxide poisoning, deaths from (P) 623
Carcinoma, *see* Cancer
Cardiac *see* Heart
Cardiology *see* Heart
Carditis *see* Heart
Care A D tetanus 1303
Carey H M appointment, 58
Cargill W P, mental retardation (C) 1328
Caries dental (LA) 1000 (Parfitt) (C) 1123 (Holding) (C) 1332
Carling Sir E R—British Practice in Radiotherapy (R) 752 British Surgical Practice (R) 288
Carminatives and œsophageal reflux (Creamer) 590
Carotid-sinus syndrome (A) 497
Carrick, J E, air-embolism and ruptured uterus 485
Carroll J D, tuberculosis (C) 49
Carter A B, functional symptoms in organic disease 908
Carter, C O genetic effects of nuclear explosions (C) 770
Carter, F B (O) 413
Cashman J M., tuberculous lymphadenitis 1286
Cassie F (O) 1081
Casson, F (O) 55 108
Casualty Department (Lowden) (R) 598
Catalase (LA) 238
Catheters, occluding Foley (Matheson) (C) 1179
Cathie I A B, toxoplasmosis (C) 149
Causalgia (A) 602
Cave A J E osteo arthritis of Luschka joints 176
Cawadias A P sanatoria (C) 155
Cells *see* Cytology
Central African Journal of Medicine 313
Central Council for Health Education 978
Central Health Services Council 314, 1117 1170
Central Midwives Board 926
Centre for Spastic Children 1320
Centrifuge man-carrying 1066
Cerebellar degeneration (A) 444
Cerebral *see* Brain
Cerebrospinal fluid *see* Brain
Certificate in public health, abandonment of, 1171
Cetyl trimethylamine bromide sterilisation of blankets with (Blowers and Wallace) 1250
Challenge of Man's Future (Brown) (R) 952
Challenger, F, fœtor hepaticus, 1239
Chalmers, J A., anuria, 79
Chalmers, J N M, anæmia (C) 772
Chapman H short frenula of lips and tongue (C) 871
Chapman Huston, D Through a City Archway, 573
Chelating agents (LA) 754
Chemistry—chelating agents (LA) 754, Chemical Pathways of Metabolism (Greenberg) (R) 83 Chemistry and Biology of Pteridines (Wolstenholme and Cameron) (R) 654, *see also* Biochemistry
Chemotherapy—crippling dyspnœa due to in pulmonary tuberculosis (Slade) 1203, long term, of tuberculosis (Joiner, Carroll Knox, and MacLean) (C) 49 of leprosy (Jopling) (C) 101, (Lowe) (C) 254, (Corcos) (C) 514, (Worsfold) (C) 620; of pulmonary tuberculosis (A) 342, tuberculous lesions after (LA) 599
Chest—angiocardiography in diseases of (A) 1315, congenital defects of anterior wall of (A) 140 hydrothorax complicating ascites (Emerson and Davies) 487 mediastinal teratomata, sex of (Cruickshank) (C) 253, Practical Manual of Diseases of Chest (Davidson and Friend) (R) 236, reducing observer error in 70 mm chest-radiography service for general practitioners (Stradling and Johnston) 1247, routine preoperative radiography of (Loder) 1150, tuberculous pleurisy (A) 1162, *see also* Bronchi, Heart, Lungs
Chiari's syndrome (A) 710
Chickenpox virus, 544
Chief Inspector of Factories, report of for 1953, 94
Childbirth *see* Labour
Children—A B C of Food and Child Feeding (Clark) 1230, achalasia of cardia in adolescents presenting with respiratory symptoms (Davies and Roberts) 840, aged less than 5 years, health and growth of (A) 394, allowances for (P) 350 anæsthetist looks at burnt child (Shannon) 111 (Davison) (C) 199, backward in reading (A) 658, (Jackson) (C) 822, child's treatment in hospital (P) 966, clinical experiments on, in hospitals (P) 54, (P) 351 (P) 412, (P) 506 corporal punishment of school children (Jackson) (C) 1027, (Angel) (C) 1125, delinquent, 503, 1016 dental care for, 1269 dentists for school children (P) 412 (P) 453 Diets for Sick Children 519, Diseases of Infancy and Childhood (Sheldon) (R) 1108, education of physically handicapped, 965, Growth and Development of Children (Watson and Lowrey) (R) 492 height, weight and skeletal maturity in first 5 years of life (Acheson, Kemp, and Parfit) 691, in hospital (LA) 1110, (Hazell) (C) 1327, supervision of (ML) 1217, injections given to sleeping (Pick) (C) 53 lessons 'activity," for (Vaughan) 663, milk tablets and school-children (P) 917, orthodontic treatment for school-children (P) 54, Pædiatrics for Practitioner (Gaisford and Lightwood) (R) 704 prevention of juvenile delinquency 1016, prophylactic psychiatry in homes for (Neustatter 807, (Thompson) (C) 919 psychiatric units for in mental hospitals, 28, psychotic (A) 551 pulmonary tuberculosis, primary in (Walker) 218 rheumatic fever in 1205 slum (LA) 239, spastic care of (P) 452, spastic, clinics for, 211 spastic training of (P) 302, sweep frequency method of testing hearing of school-children (Ewing) 40, (Whetnall) (C) 163 (Ewing) (C) 255, teaching of deaf (Ingall) (C) 1226, (Owen) (C) 1330, teeth of (Lino) (C) 1274 tuberculosis in, human source of (Briggs Illingworth, and Lorber) 263, (Cox) (Hall) (C) 407, welfare of, in Glasgow, 206, with cerebral palsy, centre for 1320, *see also* Babies Horror comics Kwashiorkor
Children and Young Persons (Harmful Publications) Bill (P) 412 (P) 505
Child welfare centres, future of 504
China medicine in (James) 1068, (Berens) (C) 1226
Chlorination of water 864
Chloroplasts 159
Chlorpromazine—action of (Hopkin) 605, (Wright) (C) 724 (Hopkin) (C) 817 (Decourt) (C) 1276 adrenolytic effect of (Knox and Slessor) 790, epilepsy and (Fabisch) (C) 1277 for hiccups (A) 393 gastroscopy and (Gill) (C) 304, (Douthwaite) (C) 354, (Góndara Mazpule) (C) 512, in depression (A) 1065, (Skottowe) (C) 1129, (Rudolf) (C) 1178 in obsessive compulsive and allied disorders (Trethowan and Scott) 781, in psychiatry (Vaughan Leiberman, and Cook) 1083 (Tewfik) (C) 1179, pharmacology of (LA) 337, (Foster, O'Mullane, and Churchill Davidson) (C) 617, therapy, complications of, in 800 mental hospital patients (Lomas, Boardman, and Markowe) 1144 (Samad) (C) 1327, uses and dangers of (A) 806
Cholangiography—859 in estimation of liver function (Samuel, Gluckman and Barlow) 13, transhepatic (Patey) 102
Cholera, suprarenal glands in (De, Sengupta and Ganguli) 1043
Choriomeningitis, lymphocytic, in newborn (Komrower, Williams, and Stones) 697
Christiansen, H V L, plasma proteins (C) 1227
Christie, F H E, hypophosphatasia, 286
Christie, R V, appointment, 628
Christmas disease and hæmophilia 951
Christmas gifts, distribution of (Webb-Johnson) (C) 154
Christofi case (P) 53, (ML) 96 (P) 302
Chromatography of bacterial residues in lung lesions (Consden and Glynn) 943
Chrysops silacea 261
Church, R. E—Behçet's syndrome (C) 511, molluscum sebaceum (C) 460
Churchill Davidson, H C—chlorpromazine (C) 617 myasthenia gravis (C) 1123
Churchill Davidson, I, high pressure oxygen and radiotherapy of cancer, 1091
Circulation, *see* Blood-flow
Civil estimates (P) 453
Civilian Health and Medical Services (McNalty) (R) 850
Civil Service medical appointments (C) 1026 (Fisher) (C) 1177, (Mayne) (C) 1223
Clain, A., Physical Signs in Clinical Surgery (R) 388
Clamp, compression, for arthrodesis of first metatarso phalangeal joint (Hulbert) (NI) 597
Clapham, H I, cancer (C) 1177
Clark, F Le G—A B C of Food and Child Feeding, 1230 Ageing Men in Labour Force, 202
Clarke, E—cervical myelopathy, 171, 'Efocaine,' 896
Clarke, R—blood-loss in trauma, 629, Koltushi, 712
Clark-Kennedy A E Medicine in its Human Setting (R) 335
Clean Air Bill (A) 242 (P) 350
Clements E C (O) 1280
Climie, H, sanatoria (C) 614
Clinical Aspects of Autonomous Nervous System (Gillilan) (R) 1310
Clinical Bacteriology (Stokes) (R) 653,
Clinical Cytology (Lopes Cardozo) (R) 800
Clinical Diagnosis (Wakefield) (R) 1310
Clinical experiments (Reid) (correction) 110
Clinical Physiology of Lungs (Drinker) (R) 653
Clinical Psychiatry (Mayer Gross, Slater, and Roth) (R) 83
Clinical Significance of Disturbances in Delivery of Sweat (Sulzberger and Herrmann) (R) 850
Clinics, local authority, 667
Clinton Thomas, C L, diaphragmatic hernia 1155
Clonal ageing (LA) 656, (Platt) (C) 867
Clostridium welchii—as intestinal pathogen (LA) 390, epsilon toxin in intestinal contents of man (Gleeson White and Bullen) 384 type D recovered from man (Kohn and Warrack) 385
Coates J C, femoral hernia (C) 153
Cobalt—deficiency of, and anæmia (LA) 655 (LA) 1312, goitrogenic hazard of (James and Coles) (C) 50, successful treatment with in pure red cell aplasia (Fountain and Dales) 541, (Chalmers) (C) 772
Coburn, J G dermatitis herpetiformis 1197
Cocci, anaerobic (A) 293
Cochrane, T., atopic dermatitis (C) 568
Cœliac disease—excretion of ethanolamine-phosphoric acid in (Fisher and Neill) 334, results of late treatment with gluten free wheat diet in (Gerrard, Ross, and Smellie) 587 wheat gluten and (Ross, Frazer, French Gerrard Sammons, and Smellie) 1087
Cohen, Sir H, antibiotics (C) 46
Coito, A. tracheobronchitis (C) 873
Coitus interruptus (ML) 1272
Cold Injury (Ferrer) (R) 1158
Coles, B L, cobalt (C) 50
Collagen antigenicity of (A) 37
College of General Practitioners in Scotland, 262
Colon—diverticulitis of (A) 603, nomenclature of disorders of (LA) 705, radio

graphy of (A) 1261 ; simplified operative routine for carcinomatous obstruction of (Brooke) 945
Colonial Development and Welfare Bill (P) 350
Colonies—birth-control in (P) 54 medical appointments in (P) 500 social services in (P) 350 treatment of leprosy in (P) 765
Color Atlas of Pathology (R) 540
Colouring matter in food 88 146
Coma—diabetic intra-arterial transfusion in (Kalbag and Naish) 115°, hepatic, biochemical disturbance in (LA) 1258 ; hepatic blood-ammonium levels in (Phear Sherlock and Summerskill) 836 860, (Sevitt) (C) 1023 hepatic glutamic acid in (Walshe) 1235
Committee on hospital supplies 314
Commonwealth bursaries *1183 1232*
Compston N D Multiple Sclerosis (R) 1056

CONFERENCES AND CONGRESSES—Association of Hospital and Welfare Administrators conference 1335, European Conference on Psychosomatic Research, first, 928 National Association for Mental Health conference 716 prison medical officers and psychologists' annual conference 1134 ; Radio Isotope Conference 1954 (Johnston) (R) 545 ; Second Annual Symposium on Antibiotics (LA) 1059 Società Italiana di Ginnastica Medica national congress of, 145 Symposium on Modern Aspects of Liver and Biliary Disease 859

Congenital defects—aneurysms of circle of Willis (A) 139 Atlas of Congenital Cardiac Disease (Abbott) (R) 438, Congenital Heart Disease (Kaplan and Robinson) (R) 492 diaphragmatic hernia (Clinton Thomas) 1155 dislocation of hip arthroplasty in late treatment of 1300 dislocation of hip early clinical diagnosis of (Hindenach) 15 galactosæmia low lactose milk for (Salt, Roes, and Gerrard) (C) 1177, of anterior chest wall (A) 130 *short frenula of upper lip and tongue* (Oldfield) 528 *see also* Mongolism
Congestion, pelvic (A) 92
Conjunctivitis *see* Eyes
Conn's syndrome 1167
Connective Tissues (Ragan) (R) 800
Consciousness—Brain Mechanisms and Consciousness (Delafresnaye) (R) 800 Origins and History of Consciousness (Neumann) (R) 1157
Consden, R.—bacterial residues in lungs 913 ; plasma proteins (C) 1025
Consultants—and other specialists in hospitals 448 whole time and part time 964
Conybeare, J J—heroin (C) 1331 registrars (C) 970
Cook, L. C., chlorpromazine 1083
Cooke, A M., osteoporosis, 877 929
Cooke R. T—poliomyelitis (C) 921 struma lymphomatosa (C) 968
Cookson J S French public-health services, 665
Cooper D C. G, Luschka joints (C) 675
Cooper H A hallucinative drugs (C) 1078
Cooper N C torsion of omentum, 130
Cooper P, recognition of tablets (C) 105
Copeman, W S. C., Textbook of Rheumatic Diseases (R) 752
Corcoran, A. C., argentaffinoma (C) 198 (correction) 468
Corcos, M. G leprosy (C) 514
Cormack, M., medical care in S. African township 912
Corneal Grafting Act (Rycroft) (C) 100
Coronary *see* Heart
Corporal punishment of school-children (Jackson) (C) 1027 (Angel) (C) 1125
Corpses number of bequests of (P) 453
Corso F, erythroblastic mitoses (C) 873
Cort, J H., operations on heart (C) 153
Corticotrophin—56 and splenectomy in acquired hæmolytic anæmia (Barrie and Blackburn) (C) 205 cortisone and infection (Shaper and Dyson) 887, (Strach) (C) 1127 gel in test of adrenal cortical function (Knox and Bradfield) (C) 458 supplies available for treating acute leukæmia 415
Cortisone—56 corticotrophin and infection (Shaper and Dyson) 887 (Strach) (C) 1127 in adrenogenital syndrome (Armstrong) 1051 ; in closed crush injuries of hand (Walker) (C) 20° in exophthalmos (Medical Research Council) 6 ; in pulmonary sarcoidosis (Hoyle Dawson and Mather) 638 in tuberculous meningitis (Ashby and Grant) 85, supplies available for treating acute leukæmia, 415
Cosgrave M. J enuresis (C) 1228
Cosmetics (Harry) (R) 623
Cosmic rays—Weltraumstrahlung (Eugster) (R) 1256
Cots dangerous (A) 1261 (Herzog) (Kisch) (C) 1332
Court S. D M.—appointment 1281 staphylococcal infection in newborn (C) 969 (C) 1236
Court Brown W M. ankylosing spondylitis 1283
Courtenay Mayers B Isobel Cripps Centre (C) 257
Cowpox (Laurance) 764 (Thrower) (C) 867
Cox G L. tuberculosis (C) 407
Cozen L, Operative Orthopedic Clinics (R) 1255
Cozens Hardy J N thermonuclear explosions (C) 816
Cramond W A. uterine dysfunction (C) 566
Cramp writer's conditioning techniques in treatment of (Liversedge and Sylvester) 1147
Cranston, W I, fainting 693
Crash helmets, *1*20, (P)* 1325
Crawford N bile 1006
Creamer B œsophageal reflux 279 and carminatives 590
Crew, F A E Army Medical Services (R) 1255
Cricket and calories (Fletcher) 1165
Crime—Crime Detection (Svensson and Wendel) (R) 1056 motoring offences and blood tests (P) 967 of mentally defective (Forbes) (C) 1124, (P) 1325 prevention of juvenile delinquency 1016 psychiatrists evidence in murder trials (A) 658 Roots of Crime (Fast) (R) 287 society and criminal (LA) 1159 ; young people and 503
Crimean war (Laws) 147
Cripples workshops for 109
Cripps, E C., Through a City Archway 573
Crisp E. J—hydrocortisone 476 (correction) 980 Luschka joints (C) 305
Crome L—Koltushi 713 Metchnikoff's letters (C) 1129 temporal lobectomy 882
Cropper C. F J proctitis 1283
Crosnier J Techniques de réanimation *médicale et de contrôle de l'équilibre* humoral en médecine d'urgence (R) °88
Crowe H W, phenylbutazone (C) 1076
Cruickshank, D B mediastinal teratomata (C) 253
Cryptococcus neoformans infection in man (Beck, Hutchings, Makey and Tuck) 535 (Michaels) (C) 619 (Tuck) (C) 7°4
Culture—Insanity Art and Culture (Reitman) (R) 759
Cunningham, G J appointment, 211
Currency for treatment abroad (Williams) (C) 103
Curriculum *see* Education
Cushing's syndrome *see* Pituitary gland
Cuthush M, in vivo test for incompatibility of blood 1290
Cyclopropane dental extraction and sparks (Bourne and Morton) 20
Cycloserine (A) 442
Cystinuria (Harris) (C) 720
Cystoscopy *see* Urinary bladder
Cytology—cell type in bronchial carcinoma (LA) 964, Clinical Cytology (Lopes Cardozo) (R) 800, Diagnostic cytologique du cancer génital chez la femme (Bourg Gompel, and Pundel) (R) 800 International Review of Cytology (Bourne and Danielli) (R) 387 ; sex of cancer and teratomata cells (Tavares) 918 ; sex of mediastinal teratomata (Cruickshank) (C) 253
Czoniczer G carditis (C) 678

D

d'Abreu, F hypertension (C) 409
Dales M. red-cell aplasia, 541
Daly C. infant mortality 39. 445 499
Damages—awarded to patients (Farnan) (C) 48 for rheumatoid arthritis (ML) 11°0
Danielli J F., International Review of Cytology (R) 387
Dapsone in *dermatitis herpetiformis* (Morgan, Marsden, Coburn, and Mungavin) 1197 (Alexander) 1201
Dark J tracheobronchitis 430
Darmady E M.—Hæmatological Technique (R) 335 polyarteritis nodosa, 378 sterilisation of syringes (C) 513
Davenport S G T Hæmatological Technique (R) 335
Davidson M.—Brompton Hospital (R) 63 Practical Manual of Diseases of Chest (R) °38
Davidson, S. Negroes in U.S.A. (C) 719
Davies D., achalasia of cardia 840
Davies H E. F fate of intravenous potassium, 1097
Davies J H M. handicapped adult 1212
Davies J H hydrothorax complicating ascites, 487
Davies, J N P Kwashiorkor (R) 492
Davies-Colley R death of 855 (O) 924
Davis N electric blanket (C) 710
Davis T and L. Doctor to Islands, 8 5
Davis W S, overhydration and underhydration (C) 107,
Davison, G burnt child (C) 199
Dawson J sarcoidosis 638
Dawson Edwards, P theatre-spotlight (NT) 519
De S N., cholera, 1043
Dean R. F A Kwashiorkor (R) 492
Deaths from—diphtheria since 1915 661 *gas poisoning* (P) 823, *see also* Mortality
Debray C. Maladies de l'intestin et du péritoine (R) 90°
Decourt, P chlorpromazine (C) 1270
Delafresnaye J F Brain Mechanisms and Consciousness (R) 800
Delinquency *see* Crime
Delivery *see* Labour
Demographic Yearbook *1954 864*
Dent C. E phosphoethanolamine 131
Dental *see* Teeth
Dentists—for school-children (P) 412 (P) 458 pay of, 875 (P) 917 recruitment of (P) 514 shortage of 979
Dentures immediate (A) 1310
Depression treated with drugs (A) 1065 (Skottowe) (C) 1129 (Rudolf) (C) 1178
Dermatitis, *see* Skin diseases
Dermatology *see* Skin diseases
Dermatoses, *see* Skin diseases
Desandre M. shock (C) 1234
de Sèze S Maladies des os et des articulations (R) 438
Detergents in resuscitation of newborn (A) 601
Deucharr A (O) 105
Deuterium (A) 393
Deutsche Medizinische Wochenschrift 1181
Development of Tropical and Subtropical Countries (Banks) (R) 654
Développement psycho moteur du premier âge (Koupernik) (R) 438
de Wardener H E—estimation of blood loss (C) 1125 polyarteritis nodosa, 378 ; tubular *necrosis*, 580
Dexamphetamine sulphate in depression (A) 1065
Dexter F freeze-drying arteries 858
Dextran, *see* Iron
Diabetes mellitus—blood levels of pyruvic acid and of α ketoglutaric acid in (Smith and Taylor) 27 diabetic ketosis hazards in treating (LA) 549 ; Diabetic Life (Lawrence) (R) 1256 hypoglycæmic effect of dimercaprol in diabetics with insulin resistant hyperglycæmia (Butterfield) 489 hypophysectomy in (A) 1314 intra-arterial transfusion in diabetic coma (Kalbag and Naish) 1162 low-fat diet and therapeutic doses of insulin in (Singh) 422 neuropathy in (Matthews) 474
Diacetylmorphine (P) 453
Diagnosis—Clinical Diagnosis (Wakefield) (R) 1310 Dental and Oral X Ray Diagnosis (Hutchinson) (R) 800 Diagnosis and Treatment of Acute Phase of Poliomyelitis (Bower) (R) 1255 Diagnostic Advances in Gastrointestinal Roentgenology (Bendick) (R) 1006, Diagnostic cytologique du cancer génital chez la femme (Bourg Gompel and Pundel) (R) 800 Diagnostic électrocardiographique (Jouve Senez and Pierron) (R) 1310 early clinical of congenital dislocation of hip (Hindenach) 15 of active carditis (Czoniczer and Szabó) (C) 678 of appendicitis (Kerr) 736 (Keizer) (C) 972 (Horwitz) (C) 10°7 (Kerr) (C) 1279, of pericardial effusion (A) 91 (correction) 160, of rheumatic valvular disease 19°4–61 (Bramwell) 213, of tumours of glomus jugulare (Holesh) 169, (Bickerstaff) (C) 255
Diaminophenylthiazole (A) 737
Diaminopimelic acid (Consden and Glynn) 913
Diamorphine hydrochloride *see* Heroin
Diamox *see* Acetazoleamide
Diaphragm—traumatic rupture of (Sinha) *1001 (A) 1012 see also Hernia*
Diarrhœa of babies, *Bact coli* in (Ogawa and Ogawa) (C) 671
Dickins, A M. laparotomy wounds (C)
Dickinson, C. J hospital staffs (C)
Dick H V, predicament of family
Dickson J W cold baths (C) 564
Diesel oil dangers of 1.°0
Diet—atherosclerosis and (Walker) Diets for Sick Children 519 gilt wheat results of late treatment cœliac disease (Gerrard R Smellie) 587 low fat and the doses of insulin in diabetes (Singh) 42° patients (L) 30 diets 1051 1181 ; restriction in (A) °03 rice (A) 3 2

Diethylcarbamazine and intestinal helminths (Dunn) 592
Digby G W, Meaning and Symbol 926
Digital Circulation (Mendlowitz) (R) 1057
Dihydroxyphenylisatin (A) 1261
Dimercaprol hypoglycæmic effect of in burnt patients and in diabetics with insulin resistant hyperglycæmia (Butterfield) 489, (Rios Mozo) (C) 973
Dimethanesulphonyloxybutane in chronic myeloid leukæmia (Galton and Till) 425
Dinners—Association of British Pharmaceutical Industry annual dinner, 927, British Association of Physical Medicine annual dinner, 928, *Buckston Browne* Gray Hill dinner 1082, Faculty of Anæsthetists 7th anniversary dinner, 730 Goligher, Prof J C, dinner to, 362 Hunterian Society annual dinner, 414, Lloyd, Dr W E dinner to 262, Medical Society of London 175th anniversary dinner, 628 Royal College of Surgeons of England Hunterian Festival dinner, 414, Royal Society of Medicine 150th anniversary dinner, 1282
Diphtheria notifications and deaths since 194, 561
Directory of Convalescent Homes, 465
Disabled—aids for 519 handicapped adult (Davies) 1212, *see also* Cripples, Rehabilitation
Disaster dealing with (Ross) (C) 865
Discombe G hæmolytic transfusion reactions (C) 99
Diseases of Infancy and Childhood (Sheldon) (R) 1108
Diseases of Nervous System (Walshe) (R) 110
Diseases of Skin (Andrews) (R) 598
Diseases of Skin (Ormsby and Montgomery) (R) 133
Disipidin' (Cosgrave) (C) 1228
Dislocations—congenital, of hip, arthroplasty in late treatment of, 1309 congenital, of hip early diagnosis of (Hindenach) 15, of eyeball (A) 92
Disodium hydrogen phosphate for tracing underground flow of water, 863
Disseminated sclerosis—(LA) 1060, and war pensions (P) 965, Multiple Sclerosis (McAlpine, Compston and Lumsden) (R) 1056
Diuresis, *see* Kidneys
Diverticulitis of colon (A) 603
Dixon, P K (O) 977
Docherty D F, mephenesin in tetanus, 437
Doctors—committee on medical man power (P) 451 826 dental extractions by 1230 doctor nurse, and hospital (A) 1062, doctor patient, and illness (Balint) 683, (Asher) 758 (Todd) (C) 816, enough ? (LA) 439, in Parliament 1168, in public health service, pay of, 964 1221 medical appointments in Colonies (P) 506 occult unemployment of (A) 240 press and, 776, telephone and (ML) 301, (P) 768
Doctor to Islands (T and L Davis) 875
Documenta Ophthalmologica (R) 84
Dodd H varicose vein stripper (NI) 1205
Doig, R S—B C G (C) 724, tuberculin tests (C) 823, tuberculosis (C) 152 (C) 620
Doll R, lung cancer (C) 1278
Dolton, E G, blood transfusion, 1052
Donald I Practical Obstetric Problems (R) 952
Donaldson M cancer 959, (C) 1177
Dornhorst, A C, respiratory insufficiency, 1185
Dott N M. lumbar plexus lesions, 688
Douglas D, hæmoglobinuria, 946
Douglas M. Koltushi (C) 970 (C) 1074
Douthwaite A H, gastroscopy (C) 354
Downie, A W Virus and Rickettsial Diseases (R) 1256
Downie, V J—jaundice (C) 675 pulmonary embolism (C) 199
Dressings—economy in 627, Nobecutane' (Ellerker) (C) 200 standardisation of textile (A) 1101
Dressler S H isoniazid resistance (C) 669
Drew, R mercury (C) 672
Drill V A Pharmacology in Medicine (R) 1107
Drinker C K Clinical Physiology of Lungs (R) 653
Drip recorder, electrical (Evans) (NI) 29
Drugs—addiction to not cruelty (ML) 911, approved names for, 1182 cost of (P) 453 economy in 627 for private patients 1218 hallucinative (Elkes, Elkes and Mayer Gross) (C) 719, (Cooper) (C) 1078 illicit traffic in (P) 350 imports of (P) 571 in N H S (P) 451 international non proprietary names of (A) 805 intraventricular administration of, 900, in treatment of depression (A) 1065 (Skottowe) (C) 1129, (Rudolf) (C) 1178 I was a Drug Addict (Street and Loth) (R) 1006 prices of (P) 1325 proprietary, classification of, 159, proprietary cost of (P) 302, Reactions with Drug Therapy (Alexander) (R) 1005 sent by post (ML) 301 sympathomimetic, antigenicity of toxoids and 950, tablets, recognition of (A) 36, (Cooper) (C) 105 (Spalton) (C) 106, tariff for, in Scotland (P) 350, *see also* Antipyretics
Dubos, R. J, Biochemical Determinants of Microbial Diseases (R) 704
Ductus arteriosus, patent, ligation of, combined with left pneumonectomy and thoracoplasty (Edge and Glennie) 796
Duguid J B, atherosclerosis 525
Dunbar F, *Emotions and Bodily Changes* (R) 850
Duncan K P rehabilitation (C) 570
Dunn, T L piperazine derivatives and helminthiasis, 592
Duodenum, *see* Intestines Peptic ulcer
Dysentery—chronic amœbic, treated with antibiotics, in combination with other drugs (Singh) 527, (Andrade) (C) 677, (Singh) (C) 1124, (Armstrong, Wilmot, and Elsdon Dew) (C) 1223, (Andrade) (C) 1224, (Lane) (C) 1331 Sonne 1216, treated with tetracycline, phthalyl sulphathiazole, and oral streptomycin (Abbott and Parry) 16
Dysmenorrhœa vitamin E in primary (Butler and McKnight) 844
Dyson, A, cortisone corticotrophin, and infection, 887
Dyspnœa, *see* Respiration

E

Ears—epidemic vertigo with oculomotor complication (Leishman) 228, sweep frequency method of testing hearing of school children (Ewing) 40, (Whetnall) (C) 153 (Ewing) (C) 255, teaching of deaf children (Ingall) (C) 1226, (Owen) (C) 1330
East, Sir N, Roots of Crime (R) 287
Eaton, J C hæmoglobinuria, 946
Eckstein, P, Technique and Significance of Œstrogen Determinations (R) 1158
Eclampsia—renal changes in (Sophian) (C) 104 treatment of, by continuous conduction analgesia (Bryce-Smith and Williams) 1241
Ectomorphy (LA) 291
Eczema nummular, treated with hydrocortisone ointment (Cochrane) (C) 568
Edge J R—hypersensitivity angiitis, 1153, pneumonectomy 796
Edinburgh, needs of aged patients in (P) 814
Education—in matters of health, 247, (Stanford) (C) 564 medical (O'Meara) 194 (LA) 903, of physically handicapped children, 965
Edwards, G sanatoria (C) 922
Edwards, L R L, poliomyelitis (C) 1223
Effective temperature scales (LA) 290
Efocaine,' spinal cord damaged by (Clarke, Morrison and Roberts) 896
Efrati P, new liver disease 538
Einstein Albert (A) 905
Eire—tuberculosis in 1221, (Pitcher) (C) 1278, *see also* Vital statistics
Elbow—golf (Crisp and Kendall) 476, Surgery of Elbow (Smith) (R) 492, tennis (Crisp and Kendall) 476
Election candidates medical 1068
Electrocardiography—as screening test (A) 805, changes after gastrectomy (Gardberg) (C) 512, changes in infarction (A) 708 Diagnostic électrocardiographique (Jouve, Senez and Pierron) (R) 1310 ruler for use in (Renfrew and Haggar) (NI) 1158, (correction) 1282
Electro-encephalography—in epilepsy (A) 1163 of boxers (A) 1114 ruler for use in (Renfrew and Haggar) (NI) 1158 (correction) 1282
Electrogastrography (LA) 190
Electrohysterography (A) 1210
Electrophoresis of serum proteins (A) 604 (Owen) (C) 868 (Consden) (C) 1025 (Miltényi) (C) 1181, (Christiansen) (C) 1227
Electro-sleep (Kerbikov) 744
Elithorn A leucotomy 23
Elizabeth Tudor (MacNalty) 520
Elkes C, and Elkes, J, hallucinative drugs (C) 719
Ellenbogen, B K, Therapeutic Index (R) 704
Ellerker A G, 'Nobecutane' (C) 200
Ellman P lungs bones and joints (C) 403
Elmes P C, bronchitis 120
Elmhirst E duodenal ulcer (C) 721
Elsdon Dew R, amœbic dysentery (C) 1223
Embolism—pulmonary (LA) 34 (Aldin) (C) 101 (Downie) (C) 199, *see also* Air-embolism
Emergency Bed Service (Abercrombie) (C) 201
Emerson P A, hydrothorax complicating ascites, 487
Emery, E W, fate of intravenous potassium, 1097
Emotions and Bodily Changes (Dunbar) (R) 850
Emphysema—interstitial in newborn 951, pulmonary (Gough) 162 action of breathing exercises in (Campbell and Friend) 325
Empire Rheumatism Council, 927
Encephalitis—mumps meningo-encephalitis and serum amylase level (Wallman and Vidor) 1105
Encephalopathy, Wernicke's (A) 91
Endobronchial *see* Bronchi
Endocardial *see* Heart
Endocrine tumour, argentaffinoma as (Page Corcoran Udenfriend, Sjoerdsma, and Weissbach) (C) 198 (correction) 466
Endocrinology—endocrine relations (Hubble) 1, endocrine response to trauma, 1055, Examen clinique et traitement d'un endocrinien (Lichtwitz and Parlier) (R) 952 Management of Endocrine Disorders of Menstruation and Fertility (Jones) (R) 1157, of reproduction 1230
Endomorphy (LA) 291
Endotracheal tube, harness for (Rolfe) (NI) 1256
Enteritis, *see* Intestines
Enuresis, *see* Bedwetting
Epidemiology—of poliomyelitis (A) 1011, prophylaxis in streptococcal epidemics (A) 553, typing in epidemiological investigations, 950, World Atlas of *Epidemic Diseases (Rodenwaldt) (R) 133*
Epididymectomy in tuberculosis (Ross Gow and St Hill) 117
Epilepsy—chlorpromazine and (Fabisch) (C) 1277, electro encephalogram in (A) 1163 genetic factors in (A) 1111 masked (Wallis) 70, (Kempton) (C) 201, (Scott) (C) 202, (Wallis) (C) 254, (Millichap) (C) 403, (Wallis) (C) 459 (Illingworth) (Ulutin) (C) 677 (O'Neill) (Wallis) (C) 725, (Ambrose) (C) 972 social clubs for epileptics, 1081, temporal lobe lesions and (Crome) 882, temporal lobe, surgery of (LA) 903, temporal lobe treated by temporal leucotomy (Falconer, Hill, Meyer, Mitchell, and Pond) 827, (Meyer) (C) 1025, visceral (A) 91
Epithelioma cuniculatum (A) 192
Erethism (Jacobides) (C) 774
Error of observer *see* Radiology
Erskine, D venereology and dermatology (C) 103, (C) 203
Erythroblasts, stimulation of mitoses of, *in bone marrow by pituitary (Marinone* and Corso) (C) 873
Erythrocytes, *see* Blood
Erythromycin—56 in staphylococcal infection of newborn (Forfar, Maccabe, Balf, Wright and Gould) 584, (Court Green, Hutchinson, and Neligan) (C) 969, (Forfar Maccabe Balf, Wright, and Gould) (C) 1071, (Hay, (C) 1127, (Court Green, Hutchison, and Neligan) (C) 1226
Escherichia coli—in infantile diarrhœa (Ogawa and Ogawa) (C) 671 stimulation of natural immunity to, in mice (Rowley) 232
Ethanolamine phosphoric acid, excretion of in cœliac disease (Fisher and Neill) 334
Ethics medical, 1219
Ethyl biscoumacetate's uricosuric action (Sougin Mibashan and Horwitz) 1191
E T scale (LA) 290
Eugster, J, Weltraumstrahlung (R) 1256
Evans F, drip recorder (NI) 29
Evans, J, Three Men 978
Evans P, Infant Feeding and Feeding Difficulties (R) 288
Evans P R C—hypertension (C) 406 virilism 436
Everidge J (O) 1280
Ewing, A. W G, testing hearing, 40 (C) 255
Ewing M, appointment 627
Examen clinique et traitement d'un endocrinien (Lichwitz and Parlier) (R) 952
Exchange Control Medical Advisory Committee (Williams) (C) 103
Exhibition—at Institute of Dermatology, 520, Ideal Home Exhibition 562, of Association of Medical Records Officers 1335 of hearing aids, 465, of Israeli scientific papers 58, of Medical Artists Association of Great Britain, 875, of Medical Art Society 804, of underwater sports, 769
Exophthalmos *see* Eyes
Experimental Psychology (Woodworth and Schlosberg) (R) 1255
Experiments clinical—design of (Reid) (correction) 110 in hospitals (P) 54 (P) 351, (P) 412, (P) 506, man as experimental animal (Jefferson) 59 on babies (P) 452, (P) 453

Explosions thermonuclear *see* Irradiation
Eyes—accidents to 94; acetazolamide in glaucoma 931, anophthalmos, cosmetic problem of (A) 240 Behçet's syndrome (Phillips and Scott) 366 boxing injuries of 1335 certification of blindness, 573 conjunctivitis, allergic, treated with hydrocortisone (Foulds Greaves Herxheimer, and Kingdom) 234 corneal grafts (Rycroft) (C) 100, cortisone in exophthalmos (Medical Research Council) 6 dislocation of eyeball (A) 92 epidemic vertigo with oculomotor complication (Leishman) 2°8 (Bickford) (C) 305, (Kuenssberg) (C) 407 (Burrowes) (C) 408 (Marshall) (C) 458 (Freedman) (Glass) (C) 674 hexamethonium and pupils (McPherson) (C) 253 Modern Trends in Ophthalmology (Sorsby) (R) 1005; Neuro-Ophthalmology (Lyle) (R) 230 ochronosis of (A) 116° optic atrophy after administration of isoniazid with *p* aminosalicylic acid (Sutton) and Beattie 650; radiography of (A) 1210, retrolental fibroplasia (*Brehmo*) (*C*) 671 *Visual Fields* (Hughes (R) 1°06

F

Fablsch, W., chlorpromazine and epilepsy (C) 1277
Face—Maxillofacial Anatomy (Shapiro) (R) 387
Factories see Industry
Faculty of Anæsthetists, 415 730
Faculty of Ophthalmologists 1183
Faculty of Radiologists 314
Fainting cutaneous vasodilatation during (Snell Cranston and Gerbrandy) 093
Falconer M. A., temporal lobectomy, 827
Fallopian tube torsion of (Abbas) 128
Fallot's tetrad *see* Heart
Family—predicament of in modern world (Dicks) 295 (Roberts) (C) 403; psychiatry 358
F.A O 465
Farnan P, patients' damages (C) 48
Fat—Fat Metabolism (Najjar) (R) 704, hardened fats and lung cancer (Yudkin) (C) 46 (Nyrop) (C) 253 (Bender) (C) 354 (Nyrop) (C) 872 (Yudkin) (C) 10°5, (Nyrop) (C) 1178 low fat diet and therapeutic doses of insulin in diabetes mellitus (Singh) 4°2
Favism (McCarthy) 748
Fawns H T, anuria, 79
Fazlullah, S hypersensitivity angiitis, 1153
Fear and appendicitis (Ribeiro) (C) 621
Fee W iron-dextran (C) 818
Feeding *see* Food
Feet—compression clamp for arthrodesis of first metatarso phalangeal joint (Hulbert) (NI) 597 epithelioma cuniculatum (A) 192 flat foot, peroneal spastic (A) 1262; Foot Faults Related to Form and Function (film) 159, shoe design and toe deformation (Pratt) (C) 106 (Sheriff) (C) 107 (Arnold) (C) 1078
Ferrer M. I. Cold Injury (R) 1158
Ferriman, D lupus erythematosus (C) 10°7
Ferritin (A) 552
Fertilisers, bone meal and anthrax (Jamieson and Green) 560
Fertility—Fertility from Town Wastes (Wylie) (R) 492 Management of Endocrine Disorders of Menstruation and Fertility (Jones) (R) 1157 of British women (LA) 138, Studies on Fertility (Harrison) (R) 704
Fibrillation, *see* Heart
Fibro-adenosis and breast cancer (A) 35 (Sancr) (C) 720
Fibroplasia retrolental (Brehmo) (C) 671
Fibrosis endocardial (*Vaishnava*) (*C*) 155
Fielding G dental caries (C) 1332
Films—film on mental nursing (Radzan) (C) 47 French prizes for medical 1032 on dental emergencies 57

FILMS.—Childbirth without Fear (Read) 1231, Foot Faults Related to Form and Function 159; Grip on the Nation, 1117 Infantile Cerebral Palsy 1117; Light through Clouds 1281 Neuromuscular Transmission in Myasthenia Gravis, 1117 Painless Childbirth (Lamaze) 1231 Rôle of Mental Function in Physical Activity 146 Troubled Mind (Radzan) (C) 47

Fingers—arachnodactyly (A) 1062 clubbed (A) 340, Digital Circulation (Mendlowitz) (R) 1057 onychodermal band in health and disease (Terry) 179 (Steer) (C) 512; reconstruction of (A) 1316 trigger-finger (A) 551 *see also* Raynaud's phenomenon
Finlayson D A., fluoridation of water (C) 868
First ten minutes (A) 757
Fischer R. schizophrenia (C) 402
Fish-and-chip shops, 146
Fishberg, A M, *Hypertension and* Nephritis (R) 1057
Fisher, A G T osteo-arthritis of Luschka joints (C) 405
Fisher H J radioactive sodium, 419
Fisher O D cœliac disease 334
Fisher, W H., Civil Service medical posts (C) 1177
Fistula—ileocolic, spontaneous, megaloblastic anæmia due to associated with subacute combined degeneration (*Wilkinson*) 74 *urinary suction-cup* for (Smith) (NI) 84
FitzGerald M G dissecting aneurysm of aorta (C) 616
Flagella, bacterial (A) 700
Flat foot (A) 1262
Flavonoids and thymus (A) 413
Flear C. T G—blood loss in trauma 620 weighing machine (C) 104
Fleming H A. Fallot's tetrad (C) 617
Fleming Sir A (O) 624
Fletcher C. M—bronchitis 120 merit awards (C) 102
Fletcher E., psoriasis spondylitica, 695
Fletcher J G, calories and cricket, 1165
Fletcher W D myoglobinuria (C) 1072
Flew R. death of 1164
Flewett T H freeze-drying of arteries, 888
Flexner, L B Gestation (R) 1108
Flora, A. tracheobronchitis (C) 873
Flour—extraction rates of (P) 10°1 1232; *see also* Agene
Fluoridation—Fluoridation as Public Health Measure (Shaw) (R) 653, of water (P) 351 (P) 412 461 (Finlayson) (C) 868
Fluoride content of water-supplies (P) 814
Fluoroacetamide, fluoroacetate and fluorocitric acid (Phillips) (C) 151
Fluorohydrocortisone (A) 853
Flynn M. P, tuberculosis (C) 461
Fœtor hepaticus (Challenger and Walshe) 1239
Fœtus infection of (LA) 802
Fog (A) 242
Foggitt, C. H Koltushi (C) 1028, (C) 1128
Food—A.B C of Food and Child Feeding (Clark) 1°30 arsenic in 610 artificial feeding of babies (A) 443, colouring matter in, 88 146 fish and-chip shops, 146; increased expenditure on (P) 917, in mental hospitals (Hawes) 1°14, (Pulvertaft) (C) 1278 (Leitner) (C) 1330 *irradiation sterilisation of* 1323; welfare foods (P) 1022 *see also* Diet, Food poisoning
Food and Agriculture Organisation 465
Food Hygiene Advisory Council 979
Food poisoning (P) 571 (A) 709
Foot *see* Feet
Foot-and mouth disease (P) 916
Forbes, R. professional secrecy (C) 1124
Forfar J O, staphylococcal infection 584 (C) 1071
Forrest, A. P M. pituitary radon implant 1054
Foss, G L impotence (C) 252
Foster C. A., chlorpromazine (C) 617
Foster-Carter A F, sanatoria (C) 508
Fothergill, C F (O) 1080
Foulds W S hydrocortisone °34
Foundations of Surgery (Perkins) (R) 235
Fountain J R. red-cell aplasia 641
Fourman, P potassium and tetany 329
Fowler I B S.—hypertensive heart failure 417 rehabilitation 407
Fox E D sulphonamide sensitivity (C) 203
Foxell A. W H thrombocytopenic purpura, 1053
Frame H F enteritis, 435
France—public-health services in (Cookson) 665 smallpox in 147 206 248 351 410
Franceschini P Si tema Istiocitario (R) 701
Francis A E vaccine lymph and aureomycin (C) 872
Fraser D hypophosphatasia 280
Fraser R. n.m.n. during sleep, 632
Frazer A C, cœliac disease 1087
Fraser J I D melanophore-expanding activity of pituitary gland (C) 513
Freedman B—Behçet's syndrome (C) 569 epidemic vertigo (C) 674
Frei, W Brucellose als Anthropo Zoonose (R) 438
French J M. cœliac disease 1087
Frenula short of lips and tongue (Oldfield) 828, (Pickerill and Pickerill) (C) 773 (Chapman) (van Thal) (C) 871
Frew R. S. (O) 12°9
Friedl E. Roentgen Diagnostics (R) 186
Friedmann I B.C.G (C) 869
Friend J H—Practical Manual of Diseases of Chest (R) 236 pulmonary emphysema 3°5
Fry, J influenza (C) 250
Fryer, D I. Comet aircraft disasters 1135
Fumigation of perambulator caused baby's death (ML) 912
Funchal, British cemetery at 561
Fundamentals of Psychoanalytic Technique (Brantey) (R) 330
Fundamentals of Radiology (Bacq and Alexander) (R) 902

G

Gaisford W Pædiatrics for Practitioner (R) 704
Galactosæmia, low-lactose milk for (Salt, Ross, and Gerrard) (C) 1177
Galinier F., shock (C) 1224
Gall bladder and heart block (A) 1164
Galpine J F.—artificial positive pressure respiration (C) 7°2, positive-negative pressure respirator 1209
Galton D A G, myeloid leukæmia 425
Gándara Marpule L gastroscopy (C) 513
Ganguli N C. cholera 1043
Gardberg M, gastrectomy (C) 512
Garland, J Physician and His Practice (R) 1157
Garland, T O Artificial Respiration (R) 545 1323
Gas-cylinder trolleys, British standard 1032
Gas poisoning number of deaths from (P) 6_3
Gastrectomy, *see* Stomach
Gastric, *see* Stomach
Gastro intestinal *see* Stomach
Gastroscopy *see* Stomach
Gatenby P B B anæmia in pregnancy 740
Gehl R H Graphomotor Projection Technique (R) 598
Geisteskraft und Geistesstörung im Alter (Kielholz, Stoll, Vischer Buel, and Wyrsch) (R) 1058
Gelin, G, La rate et ses maladies (R) 346
General Board of Control for Scotland, 826
General Medical Council 1117, 1171
General Medical Services Subcommittee (Scotland) 58
General practice—1°18 anæmia in 82 assistants in 1219 group practice loans (P) 814 in Scotland 299 Into General Practice (Thwaites) (R) 186; Physician and His Practice (Garland) (R) 1157 research in (LA) 953
General Practice Reform Association 1134
General practices, geography of 116 (Hadfield) (C) 358
General practitioners — holidays of (Stewart) (C) 620 in N H.S (P) 966 reducing observer error in 70 mm. chest-radiography service for (Stradling and Johnston) 1247 state of surgeries of (ML) 1010
Genetics—disseminated sclerosis (McAlpine) 1033 (LA) 1060 epilepsy (A) 1111 Genetica Medica (R) 1°06 investigation of inherited factors in disease 544 Marfan's syndrome (arachnodactyly) (A) 106° of bacteria 145 rheumatic fever (A) 490 (Wilson) (C) 11°4 *see also* Irradiation
Genito-urinary—infections with hæmophilus (A) 141, tuberculosis, treatment of (Ross, Gow and St Hill) 116 (Haines) (C) 203 (Gow) (C) 456
Gerbrandy J fainting 693
Geriatrics *see* Aged
Germany—health services of West 1215; rabies in (A) 30 (Wells) (C) 674 (Hemmes) (C) 824
Gerrard, J W—appointment 6°8 cœliac disease 587 1087 galactosæmia (C) 1177
Gestation *see* Pregnancy
Gibberd G F labour ward bed (NI) 901
Gibbs M., journals for overseas (C) 7°5
Gibson J B achalasia of cardia (C) 069
Gibson K. B work of geriatric unit 960
Gibson Q H appointment, 631
Gibson T, lymphœdema præcox (C) 156
Giles, H M.—hospital staffs (C) 8°0; lead poisoning 163
Gill A. M, gastroscopy (C) 304
Gillet J A lead poisoning 1118
Gillhespy, R O vitamin B_{12} (C) 1078
Gillilan L A Clinical Aspects of Autonomic Nervous System (R) 1310
Gillis, L Amputations (R) 186
Giraud, R Analgésie obstétricale (R) 598
Glasse W, Sutton Coldfield railway accident (C) 562
Glaister J N war (C) 816
Glandular fever (*Hill*) (*C*) 617
Glasgow maternity and child °06

Glass, M, epidemic vertigo (C) 674
'Glassona' (Thomas) (C) 205 (Pridie) (C) 407
Glatt M M—methylpentynol (C) 308 treatment centre for alcoholics, 1318
Glaucoma acetazoleamide in 951
Gleeson White, M H *Clostridium welchii* 384
Glennie J S, pneumonectomy 796
Glomus jugulare diagnosis of tumours of (Holsch) 169
Gloves flexible lead rubber, British standard 980
Gluckman J, cholangiography, 13
Glucose see Hyperglycæmia, Hypoglycæmia
Glutamic acid in hepatic coma (Walshe) 1235
Gluten, wheat and cœliac disease (Ross, Frazer, French Gerrard Sammons, and Smellie) 1087
Glycyrrhetinic acids failure to control insufficiency of suprarenal glands (Strong and Wilson) (C) 150
Glynn, L E, bacterial residues in lungs, 943
Goff C W, Legg-Calvé Perthes Syndrome (R) 335
Goffe A P poliomyelitis, 1172
Goitre, see Thyroid gland
Golberg L iron dextran (C) 818
Goldsmith H J hexamethonium, 371
Goldsmith K antibiotics 76
Golf elbow (Crisp and Kendall) 476
Gómez F, kwashiorkor (C) 922
Gompel C Diagnostic cytologique du cancer génital chez la femme (R) 800
Gordon S, Scalpel, Sword, 57
Gordon W endobronchial tube (NI) 185
Gough J diseases of lungs, 161
Gould C A. lung cancer (C) 1180
Gould J C, staphylococcal infection, 584, (C) 1071
Gow J G, genito urinary tuberculosis, 116 (C) 456
Grafts corneal (Rycroft) (C) 100
Gramicidin (McMaster) (C) 307
'Grancodin (McMaster) (C) 307, (Lawson) (C) 404
Grange R V, hydrocortisone ointment 1038
Grant H tuberculous meningitis, 65
Grant R N R cancer (C) 1075
Graphologie et physiologie de l'écriture (Callewaert) (R) 1310
Graphomotor Projection Technique (Kutash and Gehl) (R) 598
Greaves, D P hydrocortisone, 234
Green C A staphylococcal infection (C) 969 (C) 1226
Green, D M anthrax, 560
Green R A, endobronchial tube (NI) 185
Green Armytage V B, iodised oil (C) 105
Greenberg, D M., Chemical Pathways of Metabolism (R) 83
Greenfield J G, Spino-cerebellar Degenerations (R) 30
Greenwood F rupture of laparotomy wound (C) 773
Gregory C C L Physical and Psychical Research (R) 902
Grieve J peptic ulcer (C) 308, (C) 507
Griffiths, G A (O) 1130
Griffiths J D, osteo arthritis of Luschka joints 176
Griffiths W J, polyarteritis nodosa 378
Grimson, T A, islet-cell tumour of pancreas, 334
Grip on the Nation (film) 1117
Grisley F electric blankets (C) 973
Group discussion (LA) 188
Growth—Growth and Development of Children (Watson and Lowrey) (R) 492, height weight and skeletal maturity in first 5 years of life (Acheson, Kemp and Parfit) 691 of children aged less than 5 years (A) 394
Guida Villit 262 416
Guildford J P Psychometric Methods (R) 546
Guilmant, M V, noradrenaline (C) 873
Gunther, M instinct and nursing couple, 575
Gusterson F R. tonsillectomy, 940
Gynæcology—Behçet's syndrome (Phillips and Scott) 366, Diagnostic cytologique du cancer génital chez la femme (Bourg, Gompel and Pundel) (R) 800, fertility of British Women (LA) 138, Gestation (Flexner) (R) 1108 Gynæcology (MacLeod and Read) (R) 1206 pelvic congestion (A) 92 Textbook of Gynæcology (Peel) (R) 1256 Textbook of Gynæcology (Young) (R) 388 torsion of fallopian tube (Abbas) 128, virilism due to ovarian arrhenoblastoma (Evans and Jones) 436 *see also* Labour, Maternity Menstruation Obstetrics Pregnancy Puerperium Uterus Vagina, Vulva
'Gypsona (Pridie) (C) 407

H

Haan A. M. F H, Cerebrospinal Fluid (R) 1206
Hadfield, S J, general practices (C) 358
Haeger K, poliomyelitis (C) 409, (C) 621
Hæmatite miners, lung cancer in 950
Hæmatological see Blood
Hæmoglobinuria, see Blood
Hæmophilia—and Christmas disease, 951, antihæmophilic globulin and Christmas factor deficiency in (Verstraete and Vandenbroucke) (C) 869 injury to hæmophiliac (ML) 767 surgery in (Walker) 749, (Hardisty) (C) 817
Hæmophilia Society, 979
Hæmophilus—*H influenzæ*, aerosol therapy in chronic bronchitis due to (Knox Elmes and Fletcher) 120, infections of genito urinary system (A) 141
Hæmorrhage see Blood
Hagger, I, ruler (NI) 1158, (correction) 1282
Haines M, genito urinary tuberculosis (C) 203
Hair of pilonidal sinus (Weale) 230, (Patey and Scarff) (C) 772, (Weale) (C) 821, (Page) (C) 873, (Brearley) (C) 923
Hall, G (O) 210
Hall, M tuberculosis (C) 407
Hallucinative drugs (Elkes, Elkes and Mayer Gross) (C) 719, (Cooper) (C) 1078
Hamburger J, Techniques de réanimation médicale et de contrôle de l'équilibre humoral en médecine d'urgence (R) 288
Hamdi F A. diaphragmatic hernia, 1001
Hamerton, A E (O) 359, 464
Hampshire, C H, death of, 243, (O) 310
Hancock, B J actinomycosis (C) 1123
Hand—calcium deposits in (A) 659, cortisone in treatment of closed crush injuries of (Walker) (C) 202 Manual of Hand Injuries (Nichols) (R) 1157, median nerve palsy in association with acute infection of (Bailey and Bolton Carter) 530, (Sidey) (C) 971, palmar blood supply (A) 603
Handbook for Medical Officers of Schools (R) 492
Handbook of Emergency Toxicology (Kaye) (R) 1005
Handforth C P, blood oxygen, 1252
Handler F P, cerebral arterial disease (C) 615
Hanley H G, adrenalectomy for hypertension (C) 199
Handwriting —(A) 660, (Meyer) (C) 774, Graphologie et physiologie de l'écriture (Callewaert) (R) 1310
Harding, W G, mental health (C) 457
Hardisty R M surgery in hæmophilia (C) 817
Hargreaves, E R., tuberculin testing (C) 49
Hargreaves G R—appointment, 1133, obstetrics and psychiatry, 39
Harkins H N, Billroth I Gastric Resection (R) 30
Harmer, M breast cancer (C) 670 (C) 1128
Harness for endotracheal tube (Rolfe) (NI) 1256
Harris A., neurosis 376
Harris H, metabolic disorders (C) 720
Harris R. S—Vitamins (R) 235 (R) 387, Vitamins and Hormones (R) 1005
Harris, T A. B, barbiturate antagonist, 181 (correction) 262
Harrison, C V, appointment, 1183
Harrison, L W venereology (C) 303
Harrison R G, Studies in Fertility (R) 704
Harrison T R, Principles of Internal Medicine (R) 1006
Harry R G cosmetics (C) 623
Hartley, J B, placenta prævia (C) 921
Harvey D G mercury (C) 672
Haslett Sir W (O) 55
Hathorn M, medical care in S African township 912
Hawes D G H, food in mental hospitals, 1214
Haxton, H, laparotomy wounds (C) 919
Hay J R W, staphylococcal infection (C) 1127
Haydon L J hospital reports (C) 677
Hazell, J children in hospital (C) 1328
Head—headaches (Jefferson) 60 (Wallis) 71 injuries first aid treatment of (A) 657, (Whittingham) (Romanes) (C) 775, injuries in boxing (A) 1114
Heady J A. infant mortality 343 395, 445 499 554
Heaf F R G, B C G vaccination, 315 (C) 771
Health—centres alternative to (Brooke) 93 centres at York and Stranraer 1032 education 247 (Stanford) (C) 564 978 expenditure on (A) 907, hazards and 94, in Scotland in 1954 811 occupational health service (Parker) (C) 255 of Army 450 of children aged less than 5 years (A) 394 of England and Wales in 1951, 409, of non industrial workers (P) 814, services of Northern Ireland, 1067 services of West Germany 1215, *see also* Mental health
Health Services Council 159
Hearing, see Ears
Hearing aids—exhibition of, 465 monopack (P) 54, number supplied (P) 453
Heart—adenosine and (A) 1113, adenosine triphosphate and tachycardia (Somló) (C) 1125, angina pectoris, treatment of (LA) 852, angina relieved by application of heat to precordium (Pickerill) (C) 151 (Troup) (C) 202, (Lewsen) (C) 306 angiocardiography in chest disease (A) 1315, anticoagulants in myocardial infarction (LA) 32, aortic stenosis (Bramwell) 217, (A) 906, Atlas of Congenital Heart Disease (Abbott) (R) 438 Auxiliary Heart (Wasson) (R) 653 bronchoscopic approach for measuring pressure in left auricle, pulmonary artery, and aorta (Allison and Linden) 9, Cardiac Symptoms in Neuroses (Baker) (R) 1206 changes associated with sternal depression (A) 140, Congenital Heart Disease (Kaplan and Robinson) (R) 492, coronary artery disease, 543 coronary circulation, effects of atherosclerosis on (Duguid and Robertson) 525 diagnosis of acute carditis (Czoniczer and Szabó) (C) 678, diagnosis of rheumatic valvular disease 1924–51 (Bramwell) 213 endocardial fibrosis (Vaishnava) (C) 155, failure from retention of salt and water caused by treatment with pentolinium tartrate (Rønnov Jessen) 122, (Levene) (C) 409, fibrillation, effect of anæsthesia on (Barnard) (C) 824, (Ballantine, Jackson and Wells) (Hewer) (C) 921 Heart (Luisada) (R) 84, heart block and gall bladder (A) 1164, heart failure, proteinuria due to (Segall) (C) 1276, hoarseness and coronary thrombosis (Scheuer Karpin) (C) 199, leadership in cardiology (Parkinson) 1013, massage of (Stephenson) (C) 1178, mitral incompetence (Bramwell) 216, mitral stenosis (Gough) 161 (Bramwell) 213 murmurs continuous without patent ductus arteriosus (Bonham Carter and Walker) 272, myocardial toxoplasmosis (Cathie) (C) 149 operations on (Cort) (C) 153 (Wilson) (C) 201 pericardial effusion, diagnosis of (A) 91 (correction) 160, prevention and treatment of hypertensive heart failure with ganglion blocking agents (Smith and Fowler) 417 pulmonary stenosis with cyanosis and malignant argentaffinoma (Jenkins and Butcher) 331, regulation of cardiac performance (A) 1010 ventricular fibrillation in Fallot's tetrad (Fleming) (C) 617, valvotomy for pulmonary stenosis (LA) 1160 valvotomy knife (Lentin) (NI) 134, *see also* Electrocardiography, Fainting
Heat—applied to precordium to relieve angina (Pickerill) (C) 151, (Troup) (C) 202, (Lewsen) (C) 306
Heath, E A J life assurance (C) 561
Heggie, J F radium treatment of thyroid (C) 1127
Heller, H, kwashiorkor (C) 618
Helmets crash, 1220, (P) 1325
Helminthiasis treated with piperazine derivatives (Dunn) 592
Hemmes G D, rabies (C) 824
Henry, A K, Luschka joints (C) 305
Henshaw L M E R (O) 413
Henson, G F, ruptured duodenal stump 595
Hepatic, see Liver
Hepatitis, see Liver
Heredity, see Genetics
Hernia—diaphragmatic, congenital (Clinton Thomas) 1155, diaphragmatic, following trauma (Hamdi and Sturdy) 1001, femoral repair of (Pearce) (C) 101, (Coates) (C) 153 (McElligott) (C) 405 hiatus and peptic ulcer (Johnson) 268 (C) 775 hiatus and œsophageal reflux (Creamer) 279, (Wells and Johnston) 937
Heroin—addiction to (P) 1325 ban on (P) 965 1220 (Southwood) (C) 1227, (P) 1271 (Laurence) (C) 1277 (LA) 1311, (Conybeare) (C) 1331
Herpes zoster see Shingles
Herrmann F Clinical Significance of Disturbances in Delivery of Sweat (R) 850
Hers J F P, Histopathology of Respiratory Tract in Human Influenza (R) 704
Herxheimer, H hydrocortisone, 234
Hess E V tuberculosis (C) 354, (C) 871
Hetherington, R J, research and patient (C) 1180
Hewer C L, anæsthesia and heart (C) 921

Hexamethonium—and pupils (McPherson) (C) *53; bromide in retard medium for severe hypertension (Goldsmith Beaven and Lambert) 371
Hey Groves Synopsis of Surgery (Wakeley) (R) 1157
Hibernation artificial see Hypothermia
Hiccups, chlorpromazine for (A) 393
Higgins, L G prolonged pregnancy (C) 50
Hill, A. B—aromatic amines (C) 617 clouded crystal ball (C) 872
Hill, A Bradford, lung cancer (C) 1278
Hill D temporal lobectomy 827
Hill, H B (C) 10*9
Hilliard, I M., appointment 628
Himsworth, H P leukæmia and ankylosing spondylitis (C) 280
Hinden E capital punishment (C) 455
Hindenach J C R. congenital dislocation of hip 15
Hines, E H., Peripheral Vascular Diseases (R) 1310
Hip—early clinical diagnosis of congenital dislocation of (Hindenach) 15 osteochondritis of, 1308; *see also* Arthroplasty
Histiocytes—Sistema Istiocitario (Franceschini) (R) 704
Histopathology of Respiratory Tract in Human Influenza (Hers) (R) 704
History of Medicine (Major) (R) 186
Hoarseness and coronary thrombosis (Scheuer Karpin) (C) 199
Hodge R. S enuresis (C) 867
Hoffbauer F W., Liver Injury (R) 133
Holes, knots and wires (Turner) 763 (Atkin) (C) 821
Holesh S tumours of glomus jugulare 169
Holman P, Bedwetting (R) 123
Holmes, J M. oxytocin (C) 870
Holmes, R. E anti histamines as hypnotics (C) 1331
Holstein M. H Biology of *Anopheles gambiae* (R) 131
Home care (A) 191
Homes convalescent, for London, 465
Honours—Birthday (A) 1262 1266 1321 New Year (A) 02 95; O.M. for A. Schweitzer, 498 Polar medal 574, viscounty for Sir G Huggins, 444 660
Hopkin, D A. B chlorpromazine 605 (C) 817
Hopkins, P hydrocortisone ointment (C) 1128
Horley J F leiomyosarcoma of stomach, 1305
Hormones—and cancer, 490, balance of, in allergy and immunity 1004 melanocyte-stimulating hormone (A) 392 sex, sale of 875 somatotrophic hormone in prevention of infection in patients treated with cortisone or with corticotrophin (Shaper and Dyson) 887 Vitamins and Hormones (Harris, Marrian, and Thimann) (R) 1005 *see also* Endocrinology, Osteoporosis
Horror comics (P) 412 (LA) 493 (P) 505 (Wertham) (C) 623
Horton R. L. (C) 350
Horwitz, A. appendicitis (C) 1027
Horwitz, M. ethyl biscoumacetate 1191
Hospital Costing Returns 41
Hospitals—accommodation for staff of, 169 Army (P) 453 beds for paying patients in (P) 351 building (Maidment) 397; boards of governors of teaching 1321 capital development schemes of (P) 507; Casualty Department (Lowdon) (R) 598 charges made to by private nursing homes (P) 453, children in (LA) 1110 (Hazell) (C) 13 7 children's, conversion of (A) 241 (Wells) (MacWilliam) (C) 357 (Howells) (Neville-Smith) (C) 358 (Howell) (C) 515 clinical experiments in (P) 54 (P) 351 on children (P) 412 consultants and other specialists in, 445 costing 41 costs of in Scotland 572 dental treatment and (P) 54; doctor nurse and hospital (A) 1062, Hospital Planning Requirements (Aldis) (R) 598; information from (Lee) (C) 1129, junior medical staff of (Read) (C) 461 letters from, to patients relations (ML) 97 medical establishments of (Baker) (C) 563 1270 medical reports of for industrial medical officers (Haydon) (C) 677 money for (LA) 350 (P) 412 pharmaceutical services of, 573 pharmacists shortage of (P) 412 (P) 814 pictures in wards of (A) 146 plans for new (P) 110; staffs of (Lubran) (C) 353 (McCarthy) (C) 621 (Dickinson) (C) 678 (Giles) (C) 8 0 teaching in London 975, visiting hours of (P) 412 *see also* Mental hospitals

HOSPITALS.—Belmont Hospital Sutton Surrey (A) 37; Blanchardstown Sanatorium Eire 976 Brompton Hospital (Davidson and Rouvray) (R) 83 Cardiff Maternity Hospital 1321; Cheyne Hospital for Children, London 1320 Children's Hospital Philadelphia 1*31, Crichton Royal Mental Hospital Dumfries, 28, Dewsbury General Hospital, 108* Frenchay Hospital Bristol 261 Guy's Hospital London 572 Hammersmith Hospital London, 820 1*15 Hampstead General Hospital London (P) 1*71 High Wood Hospital Brentwood Essex (Malleson) (C) 301 Hospital of St John and St. Elizabeth London, 362 Jordan Hospital Earlswood (Jopling) 856 King's College Hospital, London 1134 Lady Templer Hospital for Tuberculosis, Kuala Lumpur 1032 Merlin Park, Sanatorium Eire 979 New End Hospital London 5*2 Normansfield Mental Hospital Teddington 110 Northern General Hospital, Edinburgh, 911 Pembury Hospital Kent 1184 (correction) 1282 Princess Louise (Kensington) Hospital for Children (A) 241 (Wells) (MacWilliam) (C) 357 (Howells) (Neville Smith) (C) 358 (Howell) (C) 515 572 Radcliffe Infirmary Oxford, 109 Retreat York, 1281 Royal Edinburgh Hospital for Nervous and Mental Disorders 212 Royal National Orthopædic Hospital, Stanmore 1184 Royal National Sanatorium, Bournemouth 1230; St. Bartholomew's Hospital London 909 St Ebba's Hospital Epsom 29; St. James' Hospital Balham, 56 St. Mark's Hospital London 362, West End Hospital for Neurology and Neurosurgery London 9*6

House-officers pay of 159
Housing (Brockington) 244
Howard, C viper broth (C) 202
Howell, B W children's hospitals (C) 515
Howells J G children's hospitals (C) 358
Howells L H Amphetamine in Clinical Medicine (R) 902
Hoyle C sarcoidosis 638
Hubble D—endocrine relations, 1 regional hospital boards, 711
Hudson, B pituitary gland, 386, (C) 775
Hughes B Visual Fields (R) 1206
Hughes D O sanatoria (C) 203
Hughes, K E. sterilisation of syringes (C) 513
Hulbert K F compression clamp for arthrodesis of first metatarso phalangeal joint (NI) 397
Human Adrenal Cortex (Wolstenholme and Cameron) (R) 1108
Human Limbs and their Substitutes (Klopsteg and Wilson) (R) 752
Humble J G poliomyelitis vaccines (C) 973
Humby knife modified (Braithwaite) (NI) 1004
Hunter D mercury (C) 872
Hunter J D adrenocortical secretion, 884
Hunter W, caravan sites (C) 1128
Hutchings, M. W, torulosis 535
Hutchinson, A. C W, Dental and Oral *X Ray Diagnosis (R) 800*
Hutchinson, J R. (C) 1130
Hutchison J G P staphylococcal infection (C) 969 (C) 1226
Hyaline membrane in lungs of newborn (Lynch and Mellor) 1002
Hyaluronidase (Lydon) (C) 918
Hydergine (Rollason) (C) 256 effect of, on uterine action (Jeffcoate and Wilson) 1187 (Bayly) (Jeffcoate and Wilson) (C) 1329
Hydrocortisone—56 by local injection, 1117; in allergic conjunctivitis, allergic rhinitis and bronchial asthma (Foulds, Greaves, Herxheimer and Kingdom) 234 in lesions of soft tissue (Crisp and Kendall) 476 (correction) 980 (Tempest) (C) 569 intravenous (Nabarro) (C) 252 ointment assessment of results of treatment with (Russell Pegum Thorne and Grange) 1038; ointment in dermatoses (Cochrane) (C) 568 (Hopkins) (C) 1128
Hydrothorax complicating ascites (Emerson and Davies) 187
17 Hydroxycorticosteroids plasma level of in pregnancy (Bayliss Browne Round and Steinbeck) 62
4 Hydroxyisophthalic acid (A) 342
Hydroxystilbamidine in—actinomycosis (Hancock) (C) 1123 thrush œsophagitis (Wolff Petty Astley and Smellie) 991
Hymenolepis nana (Dunn) 593
Hyperglycæmia after burns (Sevitt) (C) 566 (Butterfield) (C) *43, (Rios Mozo) (C) 973
Hyperparathyroidism and peptic ulcer (A) 341
Hyperpituitarism (Hubble) 1
Hypersensitivity to primary aromatic amines (Barnes and Barnes) (C) 455 (Hill) (C) 617
Hypertension—adrenalectomy for (LA) 85 (Hanley) (C) 190 (d'Abreu) (C) 409 (Menof) (C) 690 cirrhosis and portal 859 essential, and noradrenaline (Menof) (C) 204 *Hypertension and Nephritis* (Fishberg) (R) 1057 initial control of, with pentolinium tartrate (Ashby, O'Neill and Maclean) 224 (Evans) (C) 460 prevention and treatment of hypertensive heart failure with ganglion blocking agents (Smith and Fowler) 417 pulmonary (LA) 136 (Potch) (C) 400 severe treated with hexamethonium bromide in retard medium (Goldsmith, Beaven and Lambert) 371
Hypnotics, anti histamines as (A) 958 (Holmes) (C) 1331
Hypoglycæmia—due to islet-cell tumour of pancreas (Grimson and Yell) 334 fatal, in early non icteric infective hepatitis (Tomlinson) 1300 hypoglycæmic effect of dimercaprol in burnt patients (Butterfield) 469
Hyponatræmia (Cort) (C) 153
Hypophosphatasia (McCance Morrison and Dent) 131 abnormal metabolism in (Fraser Yendt and Christie) 280
Hypophysectomy in diabetes (A) 1314
Hypotension treated with noradrenaline (Guilmant) (C) 873
Hypothalamus *see* Pituitary gland
Hypothermia, induced—799 in newborn (Mann) (C) 613, (Smallpeice) (Jones) (C) 679 (Braithwaite) (Williamson) (Polani) (C) 773 in poliomyelitis (Brehme) (C) 156 (Rollason) (C) 250 (Haeger, Miörner and Ryd) (C) 409, (Russell) (C) 157 (Haeger and Miörner) (C) 621 in premature babies (A) 498
Hypothyroidism, *see* Thyroid gland

I

Icterogenin (Rimington) (C) 772
Identification of—newborn 211 (P) 507 tablets (A) 36 (Cooper) (C) 105 (Spalton) (C) 106
Ileocolic *see* Intestines
Illingworth R. S—epilepsy (C) 677; tuberculosis 263
Immigrants *see* Tuberculosis
Immobility innocuous temporary (Rudolf) (C) 51 (C) 675
Immunisation against poliomyelitis (A) 1011
Immunity—hormone balance in 1004; stimulation of natural, to *Esch. coli* infections in mice (Rowley) 232
Imperial Cancer Research Fund, 927
Impetigo *see* Skin diseases
Imports pharmaceutical (P) 571
Impotence (Tuthill) 124, (MacKeith) (Foss) (C) 251 (Maclay) (C) 25* (Sandler) (C) 358, (Tuthill) (C) 515
Industrial Health Advisory Committee, 681
Industrial Health and Safety Centre 729
Industrial Injuries Advisory Council 415 970
Industry—Ageing Men in Labour Force (Clark) 202 bacteria in 261 byssinosis benefit 079 Chief Inspector of Factories report of for 1953 91 health in (P) 54, hospital reports for industrial *medical officers* (Haydon) (C) 677 industrial injuries benefits 212 irradiation, protection of workers from (P) 505 (P) 768, lung cancer in hæmatite miners 950 Mental Health and Human Relations in Industry (Ling) (R) 235, *Raynaud's phenomenon* (LA) 8 (P) 415

IN ENGLAND NOW—Accreditation of hospitals 815—Allergy 1176—Americanese 454—Anson's voyage 148—Antenatal clinic in Africa, 303—*Benedict's solution* 582—*Benedict's test* 454—Bloodhound, 250—Blood's specific gravity 668—British Cemetery, Funchal 561—Burns Robert 219—Buses in London 1070—Canine somatotypes 1274—Cats 10, 250 303 352, 401, 1328—Central heating 454—"Child Guidance" 13 6—Children and hospital, 112*—Coca-Cola 45—Colorado 97—Comics 454—Conductors longevity of 908—Consultant's letter 612—Consultation 10*2—Cormorant catching 45—*Cricket 122*—Death certificate 6**—*Definitions 505—Driving test in U.S.A 1132—Dyes 668—Election, 1170—Epsom 11 6—F tal 613—Evans the Rectum 11*3—Examination for C P H 148—Fallen navel 14*—First night 852—Fluoridation 718—Fountain in Queen

Square, 352—French 507—Handkerchiefs, 1070—Heat barrier 760, 865—'Highers' 613—Hospital garden 1326—Hospital porter 508—House work, 917—Hydroxypopyl nor yenwupongine, 917—Hypnotics 45—Ideal Home Exhibition 562—"I like to go to Guidance Clinic" 98—'I m glad you like the Guidance Clinic 148—'Interlude," 1273—Key to Kingdom of Heaven, 96—Khartoum sanitation 401—'Lie on your back on the couch" 968 1023, 1122—Medical Art Society's exhibition, 864—Medicines, ward, 454—Middle East 1022—Mother's night, 718—Motor-car as biological hazard, 918—Motoring in 1902, 865—Mumps orchitis 668—Mushroom poisoning, 967—National economy, 507—*National Formulary*, 249—News from school, 454 1274—Newspaper strike, 815—'O & M 148—Paraffin, 401—Patient, last, 612—Patients, 1222, and doctors in hospitals, 1070—Penicillin, 45—Permutations 401—Plumbers 1070—Poliomyelitis vaccines, 864—Political endocrinology 1122—Post mortems 1274—Quince 1222—Railway strike 1222—Rats, 769—Red tape 303—Rhubarb farm 352—Royal Academy, 967—Royal College of Physicians 1122—Rural difficulties, 302—Scurvy 148—'Sir John Bland Sutton," 865—'Song of a Demi-centenarian," 1070—Sonnet to Neglected Organs,' 918—Spain 1070, 1273—Stethoscope siphons petrol 1176—Surgical Polypharmacy,' 198—Sympathy marital, 1176—Taxi-drivers of New York, 612—Telephone calls, 718—Televideosuggestive psychotherapy, 401 Telling doctor 815—Trousers 98—Uncle Tom Cobbleigh and all 198—Underwater sport 769—W c 1326—Worms, 250

Infants see Babies
Infarction—electrocardiographic changes in (A) 708, myocardial anticoagulants in (LA) 32
Infection—before birth (LA) 802 chronic, causing osteosclerosis (Weber) 386 cortisone corticotrophin and (Shaper and Dyson) 887, (Strach) (C) 1127, protective function of gastro intestinal tract against, 1004 susceptibility to 1004 vascular phenomena in, 1004 see also Staphylococci
Infections—(A) 709, acute, of respiratory tract (LA) 289 vitamin C and (A) 443
Infectious diseases, monthly lists of 147, 361 813 1019 1270
Influenza—248 300 (Fry) (C) 356 610 Histopathology of Respiratory Tract in Human Influenza (Hers) (R) 704 virus, direct flocculation of (Bolyavin) 698
Infusion apparatus, constant (Josephs and Schmieden) (NI) 388
Infusions into bone marrow (A) 604
Ingall B I deaf children (C) 1226
Injections given to sleeping children (Pick) (C) 53
Insanity—(LA) 1259, Insanity, Art and Culture (Reitman) (R) 752 psychotic children (A) 551, see also Psychiatry Schizophrenia
Insecticides—insecticidal lacquer (Metallurgical Chemists Ltd) (C) 257, resistance to (A) 497
Instinct and nursing couple (Gunther) 575, (Jelliffe) (C) 1024
Institute of Cardiology, London 979
Insulin see Diabetes
Intelligent Teacher s Guide to Preferment (Rose) 730
Interlingua, 361
Intermedin (A) 392
International College of Surgeons, 110
International Review of Cytology (Bourne and Danielli) (R) 387
International Society for Human and Animal Mycology 1032
Intervertebral-disc syndrome, stress as factor in (A) 710
Intestines—Abdominal Operations (Maingot) (R) 1158, *Clostridium welchii* as pathogen in (LA) 390 *Cl welchii* type D recovered from human (Kohn and Warrack) 385 Diagnostic Advances in Gastrointestinal Roentgenology (Bendick) (R) 1006, disturbances of small bowel after abdominal operations (Bourne) (C) 51 duodenal stump rupture of, after gastrectomy (Henson) 595 (Warren) (Schofield) (C) 721 (Lunn and Noon) (C) 823, (Stammers) (C) 923, enteritis drug induced (Frame and Short) 434 helminthiasis treated with piperazine derivatives (Dunn) 592, ileocolic fistula spontaneous megaloblastic anæmia due to associated with combined degeneration of spinal cord (Wilkinson) 71 Maladies de l intestin et du péritoine (Rachet Busson and Debray) (R) 902, obstruction of, *Cl welchii* and (Gleeson White and Bullen) 384 obstruction of in newborn (A) 292, primary peptic ulcer of jejunum (Levitt and Saint) 77, proctitis, idiopathic granular (Cropper) 1253 protective function of gastro intestinal tract against infection, 1004, recording movements of (LA) 189, Surgery of Small and Large Intestine (Mayo) (R) 1108 X ray Atlas and Manual of Esophagus Stomach and Duodenum (Meuwieson) (R) 1157 see also Appendicitis, Colon, Diarrhœa, Dysentery Steatorrhœa Stomach
Into General Practice (Thwaites) (R) 186
Intrarenal, see Kidneys
Intravenous infusions thrombophlebitis following (Morris) (C) 154, (Banerji) (C) 514
Intrinsic factor, see Stomach
Iodised oil, reactions to (Green Armytage) (C) 105
Ireland, see Eire, Northern Ireland
Iron—as liver poison (A) 552 deficiency of and anæmia (LA) 655, deposition of, in testes, after administration of iron dextran (Nissim) 701, (Golberg Fee, and Martin) (C) 818 (Macgregor) (C) 1074, iron dextran reactions to (Ross) (C) 51, see also Anæmia, Hæmatite miners
Irradiation—Fundamentals of Radiobiology (Bacq and Alexander) (R) 902, nuclear, defence against (P) 727, nuclear, effects of (A) 707, (P) 725, (P) 768, (Carter) (C) 770 (Kershaw) (Cozens Hardy) (C) 816, (Bourdillon) (C) 866 (Pirie) (C) 918, (A) 1012 1231, protection against (A) 294 protection of workers from (P) 505 (P) 768, Radiobiology Symposium 1954 (Bacq and Alexander) (R) 545, ultrasonic of frontal lobes (A) 38 uses of, 1323, see also Radiotherapy
Isaac and Œdipus (Wellisch) (R) 438
Isaacs B acetazoleamide 995
Isobel Cripps Centre (Barlow) (C) 156, (Meyer) (Neil) (C) 206, (Courtenay Mayers) (Barlow) (C) 257 (Neil) (C) 308, (Barlow) (C) 358
Isoniazid—derivative (Bavin, Kay, and Seymour) (C) 303, in primary pulmonary tuberculosis (Todd) 794, optic atrophy after administration of *p* amino salicylic acid and (Sutton and Beattie) 650 resistance to (LA) 238 use of (Wijesekera) (C) 407, see also Tubercle bacilli
Isotopes radioactive — erythrocytes labelled with, in testing for incompatibility of blood in vivo (Mollison and Cutbush) 1290 Radio isotope Conference, 1954 (Johnston) (R) 545
I was a Drug Addict (Street and Loth) (R) 1006

J

Jackson D —backwardness in reading (C) 822 corporal punishment (C) 1027
Jackson, I, anæsthesia and heart (C) 921
Jackson R N, shingles (C) 52
Jacobides, G M, erethism (C) 774
Jamain, B Analgésie obstétricale (R) 598
James, D W Chinese medicine 1068
James E F tuberculosis (C) 251 (C) 771
James U, cobalt (C) 50
Jamieson, W M anthrax 560
Jaundice—(Downie) (C) 675 859, caused by extract of *Lippia rehmanni* (With) (C) 618 (Rimington) (C) 772, (With) (C) 1026 prolonged, with unidentified pigment in liver cells (Klajman and Efrati) 538 (Stransky) (C) 1227
Jaws—Maxillofacial Anatomy (Shapiro) (R) 387
Jeffcoate T N A, Hydergine,' 1187, (C) 1329
Jefferson Sir G, man as experimental animal, 59
Jejunum, see Intestines
Jelliffe D B—instinct and nursing couple (C) 1024, malnourished community (C) 149
Jenkins, J S, argentaffinoma 331
Jennings D gastrectomy (C) 356
Jewsbury, P tracheobronchitis 430
Johnson H D gastric and duodenal ulcers 266 (C) 775
Johnston J E, Radio isotope Conference, 1954 (R) 545
Johnston, J H hiatus hernia 937
Johnston R. N chest radiography 1247
Joiner C L tuberculosis (C) 49
Joint Consultants Committee—meeting 399 statement about senior registrars 94
Joints—bones and lungs (A) 340 (Ellman) (C) 403 Maladies des os et des articulations (de Sèze and Ryckewaert) (R) 438 see also Arthritis, Arthrodesis, Behçet's syndrome Elbow, Hip
Jonas, K C Babcock's Principles and Practice of Surgery (R) 387
Jones, G S, Management of Endocrine Disorders of Menstruation and Fertility (R) 1157
Jones, H E hypothermia (C) 679
Jones, R. N, ligature winder 627
Jones, R O, virilism 436
Jopling, W H—chemotherapy of leprosy (C) 101, leprosy in Britain 856
Jordan, A—inaccuracy in laboratory (C) 774, merit awards (C) 152
Josephs, M, infusion apparatus (NI) 388
Journals—*Archivos de Neurobiologia*, 112—*British Journal of Anæsthesia*, 1230—*British Medical Bulletin*, 485—*Deutsche Medizinische Wochenschrift* 84, 600, 1184—*Documenta Ophthalmologica* 1257—for overseas (Gibbs) (C) 725—*Lancet* (A) 853—*Medical Record* 1335—now *British Journal of Hæmatology* (A) 498 *Central African Journal of Medicine* 313—*Nursing Times* 1032—*Quarterly Journal of Experimental Physiology*, 416
Jouve A Diagnostic électrocardiographique (R) 1310
Joyce, J C, tuberculosis (C) 461

K

Kahn E, agammaglobulinæmia (C) 1075
Kahn, J H, enuresis (C) 774
Kalbag, R M, diabetic coma, 1152
Kaplan, H S, Congenital Heart Disease (R) 492
Kay E isoniazid derivative (C) 303
Kaye, S Handbook of Emergency Toxicology (R) 1005
Keating, V J, blood transfusion pump (C) 154
Keith, Sir A (O) 157
Keizer D P R, appendicitis (C) 972
Kellock, I A.—barbiturate poisoning (C) 308 yellow phosphorus poisoning, 539
Kelly, M. pain 747
Kemp, F H growth in first 5 years, 691
Kempton, J J, epilepsy (C) 201
Kendall, P H hydrocortisone, 476, (correction) 980
Kennedy, A., appointment, 314
Kent P W Biochemistry of Aminosugars (R) 1057
Ker, H R leiomyoma of stomach 1306
Kerbikov, O V, sleep in psychiatry, 74
Kerr J A, appendicitis, 736, (C) 1279
Kershaw, J D, thermonuclear explosions (C) 816
α Ketoglutaric acid, blood level of, in health and in diabetes (Smith and Taylor) 27
Ketosis, diabetic, hazards in treating (LA) 549
Khambatta, R. B F, life-assurance (C) 458
Kidneys—alkaptonuria (Harris) (C) 720 cystinuria (Harris) (C) 720 diuresis due to inhibition of carbonic anhydrase (LA) 706, (Simpson) (C) 920, (Maren) (C) 1225, Hypertension and Nephritis (Fishberg) (R) 1057, intrarenal pressure in experimental tubular necrosis (de Wardener) 580 lower nephron nephrosis, 950 nephritis, rest and activity in acute (A) 1261 pentosuria (Harris) (C) 720, Reflections on Renal Function (Robinson) (R) 850 renal acidosis, tetany complicating treatment of potassium deficiency in (Fourman and McCance) 329 renal changes in eclampsia (Sophian) (C) 104 Renal Function (Bradley) (R) 288, renal shunt in shock (Mériel, Galinier, Suc, and Desandre) (C) 1224 renal tubular failure associated with polyarteritis nodosa (Darmady, Griffiths, Spencer, Mattingly, Stranak and de Wardener) 378, tuberculous (Ross Gow, and St Hill) 116; water diuresis in primary myxœdema (Olecsky) (C) 256, see also Anuria, Uræmia
Kielholz A Geisteskraft und Geistesstörung im Alter (R) 1058
King, A, venereology and dermatology (C) 52, (C) 355
King, E mercury (C) 672
King, G M, cancer (C) 566
Kingdom L G hydrocortisone 234
Kirby, N G, sodium nitrite poisoning, 594
Kirk, E W, laparotomy wounds (C) 869
Kirkeby, K carbimazole, 374
Kirkman N F., peptic ulcer (C) 457
Kisch, H, dangerous cots (C) 1332
Klajman, A new liver disease, 538
Klopsteg, P E, Human Limbs and their Substitutes (R) 752
Knife—modified Humby (Braithwaite) (NI) 1004 valvotomy (Lentin) (NI) 134 (Slesser) (C) 514
Knight G C, leucotomy 981
Knox, B R, adrenal cortical function (C) 458
Knox, J phæochromocytoma, 790

Knox J F, lung cancer in asbestosis (C) 1275
Knox K. bronchitis 120
Knox R., tuberculosis (C) 49
Kodicek, E., maize and pellagra 898
Kohn, J *Clostridium welchii* 385
Kohsen A. Physical and Psychical Research (R) 909
Koltushi visit to (Clarke and Crome) 712 (Douglas) (C) 970 (Foggitt) (C) 1028 (Douglas) (C) 1074 (Foggitt) (C) 1128
Komrower G M. lymphocytic choriomeningitis 697
Kon S K, maize and pellagra, 898
Konstam, P G., peptic ulcer (C) 870
Koupernik, C. Développement psychomoteur du premier âge (R) 438
Kunnenberg E V epidemic vertigo (C) 467
Kuper, S W A., tuberculin and lepromin sensitivity in Bantu 906
Kutash S B, Graphomotor Projection Technique (R) 898
Kwashiorkor—573 (Williams) (C) 1071 Kwashiorkor (Trowell Davies and Dean) (R) 492 (Gómez) (C) 922, plasma electrolyte levels in (Heller and Schneiden) (C) 618 (Thompson) (C) 1181

L

Laboratory—inaccuracy (A) 604, (Bassir) (C) 677 (Jordan) (C) 774 (Wootton) (Bassir) (C) 821; services in emergencies 362, technologist (Palmer and Naylor) (C) 134
Labour—Childbirth without Fear (Read) (film) 1231 delivery by suction (A) 1315 labour ward bed for safer anæsthesia (Gibberd) (NI) 901 Mechanism of Labour (Rydberg) (R) 287 Painless Childbirth (Lamaze) (film) 1231
Labyrinthitis, acute (Leishman) 228
Lacquer, insecticidal (Metallurgical Chemists Ltd) (C) 257
adkin, R G (O) 728
dy Tata Trust 1336
maze F Painless Childbirth (film) 1231
mbert H P hexamethonium, 371
ncet, price of (A) 853
dau, E. blood transfusion pump (C) 50
R amoebic dysentery, (C) 1331
gdon Down R L. (O) 1279
nguages, foreign—(Wayne) (C) 52 (Parry) (C) 254 *see also* Interlingua
Laparotomy wounds, rupture of (Standeven) 535 (Mills) (Walsh) (C) 673 (Greenwood) (C) 773 (Oldham) (C) 810 (Kirk) (C) 860 (Haxton) (C) 919 (Walton) (Dickins) (C) 973 (Standeven) (C) 1073
Laryngeal cancer—incidence of in relation to that of bronchial cancer (Maxwell) 193 (Beales) (C) 257, (Maxwell) (C) 306 treatment of (A) 1313
Latner A L. intrinsic factor (C) 921
Lauffer, M. A Advances in Virus Research (R) 1108
Laurence B—cowpox 764 vitamin K (C) 819
Laurence, D R.—heroin (C) 1277 mephenesin in tetanus (C) 565
Lavelle H A (O) 1249
Lawrence R D Diabetic Life (R) 1260
Laws, M E. S medical mission in 1855 117
Lawson G G impetigo (C) 304

LEADING ARTICLES

Accident syndrome 547—Adrenalectomy for hypertension 85—Almoners and aged patients 600—Angina pectoris treatment of 852—Antibiotics, abuse of 1059—Anticoagulants for myocardial infarction 32—Ascites 755
Blood loss estimation of 1008—Body build and temperament 291—Bronchial carcinoma cell type in 954—By any other name, 1257
Chelating agents, 754—Children in hospital 1110—Chlorpromazine pharmacology of, 337—Clonal ageing 650—*Clostridium welchii* as intestinal pathogen, 300—Cobalt and anæmia, 655 1312—Colon disorders nomenclature of 08—Criminal and society 1150
Dental caries 1009—Diabetic ketosis hazards in treating 510—Disseminated sclerosis 1060—Diuresis due to inhibition of carbonic anhydrase 706—Doctors enough ? 439
Education, medical 903—Enuresis 391—Epilepsy surgery of temporal lobe 903
Fertility of British women 138
Gastrectomy, total 23—Group discussion 188
Heat stress indices of 290—Hepatic cirrhosis, nutritional 337—Hepatic coma biochemical disturbance in 1258—Heroic days, 87—Heroin 1311—Horror comics 493—Hospitals money for 380—Hypertension pulmonary 136
Incomplete reform, 1259—Infection before birth, 802—Insane treatment of, 1259—Intestinal movements recording of 189—Isoniazid resistance 238
Leucotomy orbital 1007—Lupus erythematosus systemic 803
Malignant disease cytotoxic agents in, 440—Man in space 801—Mental health and public health 135—Mental nursing analysed 753—Motorist, protecting the, 440
National Health Service 31—Nutrition and anæmia 655 better 1061
Parkinsonism surgical treatment of 1109—Pathology in Army century of 955—Patient thought for, 1208—Peptic ulcer: and brain 495; antacids for 1208—Peripheral nerve injuries 86—Poliomyelitis vaccines, 851 1207—Pulmonary embolism 34—Purpura, idiopathic thrombocytopenic, 494 875
Radiology observer error in, 1257—Raynaud's phenomenon in industry, 87—Research in general practice 953—Reserpine pharmacology of 548 (correction) 628—Respiratory tract acute infections of 289
Scoliosis 801—Shared responsibility 600—Slum children today 239—Spine cervical and nervous system 187—Splenic circulation 338
Tuberculous lesions after chemotherapy 599
Valvotomy for pulmonary stenosis 1160
With which we serve 31

Lead poisoning—(Turner) 662 in Rotherham (Gillet) 1119; treated with calcium disodium versenate (Giles Moore and Still) 183 (LA) 754 (Browne) (C) 775
Le Beau, J *Psycho-chirurgie et fonctions* mentales (R) 1157
Lecture Notes on Use of Microscope (Baker) (R) 438
Lee B information from hospitals (C) 1129
Lee M bladder retractor (NI) 335
Lee M. B (O) 209
Leeds Regional Hospital Board 410
Legg-Calvé-Perthes Syndrome (Goff) (R) 335
Leg Ulcers (Anning) (R) 438
Lehmann H sickle-cell trait (C) 672
Leiberman D M chlorpromazine 1083
Leiomyoma of stomach (Ker) 1306
Leiomyosarcoma of stomach (Horley) 1305
Leishman A W D, epidemic vertigo 228
Leitner Z. A. food in mental hospitals (C) 1330
Lennox B molluscum sebaceum (C) 460
Lenses, committee on 466
Lentin M valvotomy knife (NI) 134
Lepromin sensitivity in South African Bantu (Kuper) 906
Leprosy—chemotherapy of (Jopling) (C) 101 (Lowe) (C) 354 (Corcos) (C) 514 (Worsfold) (C) 620 control of 415, in Britain (Jopling) 856; in England and Wales (P) 879 treatment of in Colonies (P) 768
Lessons in ward 10 (Vaughan) 563
Leucotomy—orbital (Knight and Tredgold) 981 (LA) 1007 prefrontal (Flithorn and Beck) 23 Prefrontal Leucotomy and Related Operations (Meyer and Beck) (R) 122 Psycho-chirurgie et fonctions mentales (Le Beau) (R) 1157 temporal lobectomy for epilepsy (Falconer Hill Meyer Mitchell and Pond) 827 temporal lobectomy morphological critique of (Crome) 882, (Meyer) (C) 1025 undercutting of orbital cortex in chronic neurotic and psychotic tension states (Strom-Olsen and Northfield) 980
Leukæmia—ankylosing spondylitis and (Himsworth) (C) 250 cortisone and corticotrophin available for treating acute 415 dimethanesulphonyloxybutane in chronic myeloid (Galton and Till) 425, incidence of in ankylosing spondylitis treated with X rays (Court Brown and Abbott) 1283 Leukæmia Research (Wolstenholme and Cameron) (R) 30 respiration obstructed in acute (Levison) 1151
Levene J J, pentolinium tartrate (C) 409
Levison V B leukæmia 1151
Levitt S jejunal ulcer 77
Lewsen S C heat to heart (C) 306
Leys D war (C) 923
Lilian E. molluscum sebaceum (C) 460
Libraries *see* Books
Lichen simplex treated with hydrocortisone ointment (Cochrane) (C) 465
Lichtwitz, A Examen clinique et traitement d'un endocrinien (R) 952
Life-assurance (Khambatta) (C) 468 (Heath) (C) 564
Ligature winder (Jones) 627
Light through Clouds (film) 1231
Lightwood R Pædiatrics for Practitioner (R) 704
Lillie E W anæmia in pregnancy) 710
Lillie H R. Path Through Penguin City (R) 902
Linden, R. J measurement of pressure 9
Line E children's teeth (C) 1274
Ling T M., Mental Health and Human Relations in Industry (R) 235
Linstead Committee's report 572
Lipids—Chemistry of Lipids of Biochemical Significance (Lovern) (R) 387
Lippia rehmanni poisoning by extract of (With) (C) 618 (Rimington) (C) 772 (With) (C) 1020
Lips—congenitally short frenulum of upper lip (Oldfield) 528 (Pickerill and Pickerill) (C) 773 (Chapman) (van Thal) (C) 871
Lithium salts in manic psychosis (A) 854
Little Committee for Study of Infantile Cerebral Palsies 1183
Liver—abscess secondary to duodenal ulcer (Antia and Marker) 649 blood ammonium levels in liver disease and hepatic coma (Phear, Sherlock and Summerskill) 830 951 (Sevitt) (C) 1023 Chiari's syndrome (A) 710 cirrhosis of nutritional (LA) 337 estimation of function of by cholangiography (Samuel, Gluckman, and Barlow) 13 extract of *Lippia rehmanni* poisonous to (With) (C) 618 (Rimington) (C) 772 (With) (C) 1020, fœtor hepaticus (Challenger and Walshe) 1239; hepatic coma, biochemical disturbance in (LA) 1258 hepatic coma glutamic acid in (Walshe) 1236 hepatitis, fatal hypoglycæmia in early non icteric infective (Tomlinson) 1300; iron poisonous to (A) 552 Liver Injury (Hoffbauer) (R) 133 new disease of (Klajman and Efrati) 538 symposium on diseases of 869 tuberculosis of atypical (A) 806
Liversedge, L A *writer's cramp* 1147
Llaurado J G aldosterone 1295
Lobectomy *see* Leucotomy
Locket S, mercury (C) 672
Loder R E chest radiography 1150
Löffler W Brucellose als Anthropo Zoonose (R) 438
Loiasis 461
Lomas J chlorpromazine, 1144
London—control of health services of, 1175 convalescent homes for 405; pay of chief officers of L.C.C, 302, radioactivity of air in (P) 814 Report of County Medical Officer of Health and School Medical Officer 1953 93 teaching hospitals in 978 vaccination against smallpox in 965, water-supply of 863 *see also* Vital statistics
London School of Hygiene and Tropical Medicine 465 1134
London University Institute of Child Health 1170
Lopes Cardozo P Clinical Cytology (R) 800
Lorber, J tuberculosis 283
Lord Nuffield Fund for Cripples 776
Loth, D I was a Drug Addict (R) 1096
Lovell H R H appointment 627
Lovern J A. Chemistry of Lipids of Biochemical Significance (R) 387
Low J B (O) 413
Lowden T G Casualty Department (R) 598
Lowe J leprosy (C) 354 (O) 1080
Lowenfeld M—enuresis (C) 1026, Lowenfeld Mosaic Test (R) 338 (C) 671
Lowrey G H, Growth and Development of Children (R) 492
Loxton G E M.C.O (O) 519
L.S D 25, *see* Lysergic acid diethylamide
Lubran, M hospital staff (C) 353
Luder, J mongols (C) 6[illegible]
Luisada A, Heart (R) 84
Lukose G M. (O) 359
Lumb, G Tumours of Lymphoid Tissue (R) 30
Lumleian lectures (Cooke) 877 929
Lumsden, C E Multiple sclerosis (R) 1056
Lungs—bones and joints (A) 310 (Filman) (C) 403 cancer of (Stross) (McClean) (C) 53 (Ball) (C) 155, cancer of in asbestosis (A) 1163 (Knox) (C) 1275 cancer of in hæmatite miners 950, cancer of hardened fats and (Yudkin) (C) 46 (Nyrop) (C) 253 (Bender) (C) 354 (Nyrop) (C) 872 (Yudkin) (C) 1025 (Nyrop) (C) 1178 cancer of mortality of (P) 960 cancer of smoking and (A) 392, (Mims) (Gould) (C) 1180 (Doll and Hill) (C) 1278, chemically identifiable bacterial residues in lesions of (Consden and Glynn) 913 Clinical Physiology of Lungs (Drinker) (R) 653

combined left pneumonectomy, thoracoplasty, and ligation of patent ductus arteriosus (Edge and Glennie) 706, correlation of radiological and pathological changes in some diseases of (Gough) 161 emphysema of (Gough) 162, action of breathing exercises in (Campbell and Friend) 325, hyaline membrane in of newborn (Lynch and Mellor) 1002 pulmonary embolism (LA) 34, (Aldin) (C) 101, (Downie) (C) 190 Röntgenanatomische Grundlagen der Lungenuntersuchung (Kováts and Zsebók) (R) 236, sarcoidosis of treated with streptomycin and cortisone (Hoyle, Dawson and Mather) 638 solitary nodules in (A) 1211 *see also* Pneumoconiosis Tuberculosis
Lunn, G M. rupture of duodenal stump (C) 823
Lups, S, Cerebrospinal Fluid (R) 1206
Lupus erythematosus—aplastic anæmia following mepacrine treatment of (Paton Riddell and Strong) 281 disseminated systemic (Lyell) (C) 254, (Marten) (C) 301 (LA) 803 (Ferriman) (C) 1027
Luschka joints, *see* Osteo arthritis
Luxton, R W, struma lymphomatosa (C) 968
Lydon, F L psoriasis spondylitica (C) 918
Lyell, A sulphonamide sensitivity (C) 254
Lyle, D J Neuro Ophthalmology (R) 236
Lymphadenitis peripheral tuberculous, associated with visible primary focus, natural history of (Miller and Cashman) 1286
Lymphœdema præcox (A) 38, (Gibson and Tough) (C) 156
Lynch, M J, hyaline membrane, 1002
Lynn R B Raynaud's disease, 471
Lysergic acid diethylamide (Elkes, Elkes and Mayer Gross) (C) 719, (Cooper) (C) 1075
Lyster R A (O) 1280, 1334

M

McAlpine D—disseminated sclerosis, 1043 Multiple Sclerosis (R) 1056
Maccabe A F staphylococcal infection, 581 (C) 1071
MacCallan A F death of, 768, (O) 824
MacCallum, F O, Virus and Rickettsial Diseases (R) 1256
McCallum N E W barbiturate antagonist (C) 1225
McCance R A—phosphoethanolamine, 131 tetany and potassium 329
McCarthy D J, hospital staffs (C) 621
McCarthy O R favism, 748
McClean D, lung cancer (C) 53
McCorry R L, tetracycline, 1102
McCullagh M., vaginal plug for procidentia (NI) 491
Macdonald A D, Amphetamine in Clinical Medicine (R) 902
Macdonald N, tuberculosis (C) 48, (C) 354 (C) 871
McElligott M. barbiturate antagonist (C) 820
McElligott T F, femoral hernia (C) 405
Macewen, H A (O) 1029
McGlashan, A functional symptoms in organic disease (C) 973
Macgregor A. G, iron dextran (C) 1074
McGregor D, vicarious appetite (C) 355
Mac Keith R—impotence (C) 251, Infant Feeding and Feeding Difficulties (R) 288
Mackenzie I C K taste, 377
MacKenzie K P, Operation Rangoon Jail 520
Mackenzie, M. mental health (C) 614
McKerracher D G, appointment 628
McKinnon N E breast cancer (C) 1028, (C) 1124
McKnight, E, dysmenorrhœa 844
Maclay D T, impotence (C) 252
MacLean K S tuberculosis (C) 49
Maclean M C, pentolinium tartrate, 224
MacLennan J M mental health 142
MacLeod D H, Gynæcology (R) 1206
McMaster, J impetigo (C) 307
McMaster, P E Operative Orthopedic Clinics (R) 1255
McMath W F T—accidental inoculation with poliomyelitis virus, 702 poliomyelitis neonatorum 651
MacNalty, Sir A—Civilian Health and Medical Services (R) 850, Elizabeth Tudor 520
McPherson A hexamethonium (C) 253
MacQueen, I A G, mental health (C) 457, (C) 774
MacWilliam H H, Princess Louise Hospital (C) 367
Maddison J electric blanket (C) 817
Magnus I A. chemical skin sex in Turner's syndrome, 1202
Magos L, Raynaud's phenomenon (C) 52
Maher R M, cancer, 18 (C) 512
Maidment, E, building hospitals, 397
Maingot, R, Abdominal Operations (R) 1158
Maison G L reserpine (C) 866
Maize and pellagra (Brande, Kon, Mitchell, and Kodicek) 898
Major, R H; History of Medicine (R) 186
Makey, A. R, torulosis, 535
Maladies de l'intestin et du péritoine (Rachet, Busson, and Debray) (R) 902
Maladies des os et des articulations (de Sèze and Ryckewaert) (R) 438
Malaria—361, and hepatic cirrhosis (LA) 337 in America (A) 292
Malcolmson G E (O) 517
Malleson N, High Wood Hospital (C) 304
Mallett, B L, compression of ulnar nerve 890
Malnutrition and hepatic cirrhosis (LA) 337
Man Above Humanity (Bromberg) (R) 492
Management of Endocrine Disorders of Menstruation and Fertility (Jones) (R) 1157
Manchester, lymphocytic meningo encephalitis in (Tobin) 1267
Manganese poisoning (Turner) 661
Mania, treatment of (A) 854
Mann, T, Biochemistry of Semen (R) 84
Mann T P, hypothermia in newborn (C) 613
Mann, W N steatorrhœa (C) 569
Manual of Hand Injuries (Nichols) (R) 1157
Marchiafava Micheli syndrome (Douglas and Eaton) 946
Maren, T H, diuresis (C) 1225
Marfan's syndrome (A) 1062
Marinone, G erythroblastic mitoses (C) 873
Marker F hepatic abscess 649
Markowe, M., chlorpromazine, 1144
Marriage statistics for England and Wales in 1953, 1121
Marrian, G F, Vitamins and Hormones (R) 1005
Marsden C W, dermatitis herpetiformis, 1197
Marsh, F, sterilisation of blankets (C) 1331
Marshall, C J, (O) 107
Marshall, J, spastic paraplegia, 643
Marshall, J B, epidemic vertigo (C) 458
Marson, F G W aortic aneurysm 482
Marten, R H, lupus erythematosus (C) 304
Martin, E A, reserpine (C) 1126
Martin, L E, iron dextran (C) 818
Martin, Sir C (O) 462, 518
Mason, L, physical medicine (C) 1227
Maternity in Glasgow, 206
Mather G, sarcoidosis, 638
Matheson, A T, catheters (C) 1179
Matthews, J D, diabetes 474
Mattingly, D, polyarteritis nodosa, 378
Maudsley, R. H, resin impregnated plaster of paris, 847
Maxillofacial Anatomy (Shapiro) (R) 387
Maxwell, J laryngeal cancer and bronchial cancer, 193, (C) 306
Mayer Gross, W—Clinical Psychiatry (R) 83, hallucinative drugs (C) 719
Mayne, S, Civil Service medical posts (C) 1223
Mayo, C W Surgery of Small and Large Intestine (R) 1108
Meaning and Symbol (Digby) 926
Meat, preservation of, by irradiation, 1323
Mechanism of Labour (Rydberg) (R) 287
Mediastinum, *see* Chest
Medical and Dental Defence Union of Scotland, 573
Medical examinations for seafarers (A) 853
Medical Golfing Society, 1184
Medical History of Second World War—Army Medical Services (Crew) (R) 1255, Civilian Health and Medical Services (McNalty) (R) 850, Royal Air Force Medical Services (Rexford Welch) (R) 598
Medical mission to Turkish army in 1855 (Laws) 147
Medical Record, 1335
Medical Research Council—498, (P) 768, cortisone in exophthalmos 6
Medical Register 1117
Medical Sickness Society 979
Medical superintendents of mental hospitals (P) 302
Medical Whitley Council, 159
Medicine—aviation, textbook of, adopted for use of medical officers of Royal Air Force (P) 412 Chinese (James) 1068, (Berens) (C) 1226, History of Medicine (Major) (R) 186, in Russia (Symonds) (C) 103 institutional (Spence) 41, (C) 353 Medicine in its Human Setting (Clark-Kennedy) (R) 335 Medicine, Magic and Mythology (Precope) (R) 388, Modern Trends in Psychosomatic Medicine (O'Neill) (R) 1006 Pharmacology in Medicine (Drill) (R) 1107, Principles of Internal Medicine (Harrison) (R) 1006, Story of Medicine (Walker) (R) 336, Synopsis of Medicine (Tidy) (R) 134
Medicines, *see* Drugs
MEDICINE AND THE LAW—Air embo during artificial pneumoperitoneum—Alleged libel by doctor, 767—Be death after fumigation of perm 912—Baby sent out too soon 1 Bogus doctor fined, 858—Broken in child's throat, 623—Capital ment 96—Coitus interruptus, Damages for rheumatoid arthritis, 11—Death after ambulance journey 96 Death from tetanus 680—Difficult tra fusion, 1271—Doctor's telephone 301 Drug addiction not cruelty, 911—Hab forming drug, 97—Hypersensitivity penicillin, 912—Inhaler overturned —Injury to hæmophiliac, 767—Inspe tion of surgery, 1182—Letter fr hospital, 97—Negligence action settl 813, appeal fails, 349 claim dismiss 767, what is? 400—Newspaper account of operation, 1273—Overlook swab 680—Payment for vaccinatio 507—Postal treatment, 301—Refusal bear child, 1272—State of doctors' s geries, 1019—Supervision in childre ward, 1217
'Megimide' *see* Methylethylglutarimide
Melamine formaldehyde (Maudsley) 847
Melanocyte-stimulating hormone (A) 39
Melanophore-expanding—activity of nitary gland (Hudson and Bentley) (Frazer) (C) 613, (Hudson and Bent (C) 775, hormone (A) 392
Mellanby, Sir E (O) 309, 359
Mellor, L D hyaline membrane, 100
Members of Parliament, medical, 1168
Membrane hyaline, in lungs of new (Lynch and Mellor) 1002
Memoirs of My Nervous Illness (Schre (R) 952
Mendlowitz M., Digital Circulation (R
Meninges, *see* Brain
Meningitis—tuberculous, treated cortisone (Ashby and Grant) 65 attacks of with brief interval (B 383, *see also* Choriomeningitis
Meningococci, drug resistance of (A)
Meningo encephalitis—lymphocytic, Manchester (Tobin) 1267 mumps serum amylase level (Wallman Vidor) 1105
Menof, P—adrenalectomy for hyperte (C) 620 noradrenaline and hyper sion (C) 204
Menstruation—Management of End Disorders of Menstruation and Fe (Jones) (R) 1157, urinary excre œstrogens during menstrual (Brown) 320 *see also* Dysmenorrh
Mental changes and organic d (Waggoner) (C) 105
Mental health—Mental Health and Hu Relations in Industry (Ling) (R) and public health (LA) 135 (MacLen and Small) 142, (Cameron) (C) (Wilson) (Atkin) (C) 307 (Small) (R (C) 405, (Harding) (MacQueen) (C) (Cameron) (C) 565 (MacQueen) (C) 77 and spiritual values (Vickers) 5 (Mackenzie) (C) 614, despite men retardation (Alford) 1233, research o 720, teaching of, 449
Mental hospitals—children's psychi units in, 28, day hospitals (A) 4 (Aron) (C) 734, food in (Hawes) 12 (Pulvertaft) (C) 1278, (Leitner) (C) 1 Light through Clouds (film) 1 medical superintendents of (P) 3 treatment centre for alcoholics in men hospital (Glatt) 1318
Mental nursing analysed (LA) 753
Mentally defective, carnal knowledge (Forbes) (C) 1124 (P) 1325
Mental retardation (Alford) 1233, (Car (C) 1328
Mepacrine treatment of lupus eryth tosus followed by aplastic anæmia (Pat Riddell, and Strong) 281
Mephenesin—effect of, on muscle ability (Zausmer) (C) 870, in te (Docherty) 437 (Laurence) (C) 565
Mercaptan (Challenger and Walshe) 1
Mercury—in atmosphere estimation (Hunter Bidstrup, Harvey, Bo Drew, King and Locket) (C) 673, teething powders (P) 571, poiso (Turner) 661 and pink disease (P) 6
Mériel P, shock (C) 1224
Merit awards (Fletcher) (C) 102 (Jo (C) 152 (P) 506
Mesomorphy (LA) 291
'Mestinon,' *see* Pyridostigmine bromi
Metabolism—abnormal in hypopho tasia (Fraser, Yendt, and Christie) Chemical Pathways of Metabo (Greenberg) (R) 83 Fat Metabo (Naijar) (R) 704 in schizophrenia (T and Fischer) (C) 402, of bone (C 880, *see also* Basal metabolic rate
Metacortandracin (A) 1112
Metacortandralone (A) 1112

al Chemists Ltd. insecticidal
(C) 957
h's letters to Lister and Ehrlich
(C) 1139
llene (A) 958
betamine hydrochloride in
ion (A) 1065, (Rudolf) (C) 1178
riglutarimide (Harris) 181 (cor
) 480 (Montuschi and Wickenden)
(McElligott) (C) 820 (Shaw) (C)

rcury poisoning (A) 35
tynol—and addiction (Glatt) (C)
in management of children
ing tonsillectomy (Gusterson)

n T J J H X-ray Atlas and
of Œsophagus Stomach and
n (R) 1157
A—Prefrontal Leucotomy and
Operations (R) 132 temporal
my 827 (C) 1025
F handwriting (C) 774
Isobel Cripps Centre (C) 206
of (Wilson) (C) 201
L. infections with Cryptococcus
ns (C) 610
see Bacteria
alveolaris pulmonum (Gough)

r—Lecture Notes on Use of
(Barer) (R) 438
G, isoniazid resistance (C)

National Health Service
of trichloroethylene apparatus
visits of (P) 351
treatment of (P) 870 low
for congenital galactosæmia
es and Gerard) (C) 1177
d school-children (P) 917 see
t-feeding
, Therapeutic Index (R) 704
arginine deficiency and cancer

W tuberculous lymphadenitis,

(C) 259
L aspirin poisoning, 590
G cyclical vomiting (C) 403
parotomy wounds (C) 673
plasma proteins (C) 1181
ng cancer (C) 1180
ematite lung cancer in 950
Health's statement about senior
94
Food, transfer of functions of

, poliomyelitis (C) 409, (C) 621
P leg stirrups (NI) 818
G maize and pellagra 898
temporal lobectomy, 827
Heart
atment Yearbook 1955 (Wake
50
nds in Blood Diseases (Wilkin
1107
nds in Ophthalmology (Sorsby)

nds in Psychosomatic Medicine
(R) 1000
L., in vivo test for incompati
blood 1200
pseudocarcinomatosum see
n sebaceum
sebaceum recurrent (Beare)
an and Lennox) (Church) (C)
pson) (C) 569
n Africans (Luder and Musoke)

see Thrush œsophagitis
sis, infectious (Hill) (C) 617
r H Diseases of Skin (R) 133
E, barbiturate antagonist (C)

lead poisoning, 183
) Stellate Ganglion Block (R)

D—crural ulcers 480 peptic
(C) 353, (C) 567
Billroth I Gastric Resection

I reserpine (C) 1126
vitamin K (C) 810
E. D sanatoria (C) 305
D myoglobinuria 802
K. dermatitis herpetiformis,

O death of 907 (C) 974 1030
L. Brucellose als Anthropo-
R) 438
ntagonist new (A) 757
J James Parkinson 761
thrombophlebitis (C) 134
infant mortality 313 395
354
circulation of uterine wall 323
B, phosphoethanolamine 131
Lignocaine 596
of infants, see Social and bio
ctors of infant mortality of
er (C) 966

Morton H J V cyclopropane and sparks 20
Mothers dental care for 1209
Motorists—blood tests and offences of (P) 987, protection of (LA) 440 (Rabson) (C) 819, (Bourne) 970
Mouth—Behçet's syndrome (Phillips and Scott) 366 rash on soft palate (Todd) (C) 49 see also Lips, Tongue
Muir A. pica (C) 306
Multiple Sclerosis (McAlpine Compston and Lumsden) (R) 1050
Multiple Sclerosis Society, 689
Mumps meningo-encephalitis and serum amylase level (Wallman and Vidor) 1105
Mungavin J M dermatitis herpetiformis, 1197
Murder see Crime
Murmurs continuous without patent ductus arteriosus (Bonham Carter and Walker) 272
Murphy F F meningeal carcinomatosis 231
Murray S placentography 1015
Muscles—dystrophy of (Platt) (C) 719, effect of mephenesin on excitability of (Zausmer) (C) 870 imbalance of in causation of scoliosis (Riddle and Roaf) 1245 myopathy and myositis (A) 602 see also Myoglobinuria
Music in psychiatry 619
Musoke L K. mongols (C) 693
Myasthenia gravis—Neuromuscular Transmission in Myasthenia Gravis (film) 1117 pyridostigmine bromide in (Churchill Davidson and Richardson) (C) 1123
Myelopathy see Nervous system
My Fight against Osteo-Arthritis (Orme) (R) 909
Myleran see Dimethane sulphonyloxy butane
Myocardial, see Heart
Myoglobinuria paroxysmal (Berenbaum, Birch and Moreland) 802 (Fletcher and Prankerd) (C) 1072
Myopathy see Muscles
Myositis see Muscles
Myxœdema, see Thyroid gland
Myxomatosis (P) 1325 in hare 416

N

Nabarro J hydrocortisone (C) 352
Nævi, teratomatous (Weber) (C) 155
Nagelschmidt G pneumoconiosis (C) 721
Nails see Fingers
Naish, J M. diabetic coma 1153
Najjar, V A, Fat Metabolism (R) 704
Nalorphine (P) 453
Names see Nomenclature
Nanson E., appointment 628
Nash, D F E—enuresis (C) 676 Principles and Practice of Surgical Nursing (R) 1310 tonsillectomy (C) 1378
Nash F A cancer clues (C) 507
National Association for Maternal and Child Welfare, 212
National Association for Prevention of Tuberculosis 55
National Collection of Industrial Bacteria, Catalogue of Strains, 201
National Formulary (A) 243, 219
National Fund for Poliomyelitis Research, 978 1336
National Health Service—(LA) 31 accounts 1132, estimates for 1955-56 760 National Union of Public Employees to press for 44 hour week for ancillary staff of 1134 share of Civil Estimates (P) 453 supplementary estimates, 400, (P) 451 see also Doctors, General practice, General practitioners, Hospitals Midwives Nurses Patients, Pay Prescriptions Regional hospital boards
National Insurance benefits 212
National League of Hospital Friends 608
National Service see Services
National Smoke Abatement Society 876
National Spastics Society 1052
National Union of Public Employees, 1134
Naylor P laboratory technologist (C) 154
Necator americanus (Dunn) 592
Needle broken in child's throat (MI) 623
Negligence see MEDICINE AND THE LAW
Negroes in U.S.A (Davidson) (C) 719
Neill C A Isobel Cripps Centre (C) 206 (C) 308
Neill, J H (C) 311
Neill D W cœliac disease 334
Neilson, G A staphylococcal infection (C) 909, (C) 1° 8
Neo-Mercazole see Carbimazole
Neomycin 56 in impetigo (McMaster) (C) 307
Neoplasms, see Tumours
Nephritis see Kidneys
Nephrosis see Kidneys

Nervous system—Behçet's syndrome (Phillips and Scott) 366 bilateral lumbar plexus lesions simulating cauda-equina compression (Taylor and Dott) 688 brachial plexus injuries prognosis in (A) 442 cervical myelopathy (Clarke) 171, cervical spine and (LA) 187 Clinical Aspects of Autonomic Nervous System (Gillian) (R) 1310 conditioned reflexes (Clarke and Crome) 712 Dévelopement psycho moteur du premier âge (Koupernik) (R) 438 Diseases of Nervous System (Walshe) (R) 1108, future of neurology, 131, injuries of peripheral nerves (LA) 86 metallic poisons and (Turner) 661 methyl mercury poisoning (A) 35 Multiple Sclerosis (McAlpine Compston and Lumsden) (R) 1050 Neuroanatomical Basis for Clinical Neurology (Peele) (R) 1005 neurofibromatosis and phæochromocytoma (Knox and Slessor) 790 Neuro-Ophthalmology (Lyle) (R) 136 neuropathy in diabetes (Matthews) 471 sclerosis, disseminated (McAlpine) 1037 (LA) 1060 sensory neuropathy associated with bronchial carcinoma (Smith and Whitfield) 982 ulnar nerve compressed by ganglion at wrist (Mallett and Zilkha) 890 see also Anæsthesia Brain Coma, Myasthenia gravis Pain Spine
Neuberger M. (C) 690
Neumann E. Origins and History of Consciousness (R) 1157
Neurofibromatosis, see Nervous system
Neurology see Nervous system
Neuromuscular see Nervous system
Neuro-Ophthalmology (Lyle) (R) 136
Neuropathy see Nervous system
Neurosis see Psychology
Neustatter W L psychiatry in children's homes 807
Neve R.—intra-arterial transfusion 746 rupture of duodenal stump after gastrectomy (C) 870
Neville-Smith C H Princess Louise Hospital (C) 358
Newborn see Babies

NEW INVENTIONS.—Aspiration trocar and cannula (Robson) 1309—Compression clamp for arthrodesis of first metatarso phalangeal joint (Hulbert) 597—Constant infusion apparatus (Josephs and Schnieden) 388—Electrical drip-recorder (Evans) 29—Harness for endotracheal tube (Rolfe) 1256—Humby knife modified (Braithwaite) 1001—Instrument for dividing flexor retinaculum (Paine) 654—Labour ward bed for safer anæsthesia (Gibberd) 901—Leg stirrups for cystoscopy (Mitchell) 818—Modified Magill's attachment to Boyle's apparatus (Bullough) 1309—Modified Morson bladder retractor (Lee) 335—New right endobronchial tube (Gordon and Green) 185—Orotracheal connection with minimal resistance (Bullough) 236 674—Parallel beam portable theatre-spotlight (Dawson Edwards) 819—Pilot tube for blood bottle (Campbell) 1058—Ruler for use in electro-encephalography and electrocardiography (Renfrew and Haggar) 1158 (correction) 1282—Sandal of variable height for assessing limb length discrepancies (Blockey) 960—Small urinary fistula suction-cup (Smith) 84—Throat spray modified (Swerdlow) 1004—Vaginal plug for procidentia in elderly women (McCullough) 491—Valvotomy knife (Lontin) 134—Varicose vein stripper (Dodd) 1205
Newns, G R, rheumatoid arthritis 578
Nichols H M. Manual of Hand Injuries (R) 1157
Nickels G D calliper 50
Nicol, C., venereology and dermatology (C) 148
Nigeria peptic ulcer in Southern (Smith) (C) 50 (Rose) (C) 10 Konstam (C) 8 0
Nightingale Florence (A) 110
Nisdin J, A., iron in testes, 701
Nitrogen—blood-ammonium levels in liver disease and hepatic coma (Hear Sherlock and Summerskill) 836 951 (Sevitt) (C) 1023
Nixon I viper wine (C) 232
Nixon W C W uterine dysfunction (C) 401
Nobecutane as wound dressing (Flecker) (C) 260
Nobes, P, Baytenal, 797
Nomenclature—approved names for drugs, 1132 in radiology 1184 international non proprietary names of drugs (A) 895 of disorders of colon (LA) 705
Non industrial Employment Bill (P) 614
Noon C E rupture of duodenal stump (C) 973
Noradrenaline—and essential hypertension (Mendt) (C) 901 in treatment of hypotension (Gullmant) (C) 8 2

Nordin B E C—B M R during sleep, 532 post pregnancy osteoporosis, 431, (correction) 520
Norman A G, transmetatarsal amputation, 949
Northern Ireland—births and deaths in 1953 in 94 health services of, 1067
Northfield, D W C leucotomy 986
Nose—allergic rhinitis treated with hydrocortisone (Foulds, Greaves Herxheimer, and Kingdom) 234
Notes on Transfusion (C) 205 (Bird) (C) 256
Notification of—puerperal pyrexia, 147 *tuberculosis*, 965
Notifications of diphtheria since *1945*, 561
NP13, *see* Methylethylglutarimide
Nuclear explosions *see* Irradiation
Nuffield Foundation (A) 37, 261 1183
Nuffield Orthopædic Centre 159
Nuffield travelling fellowships in medicine, 1282
Nurses—doctor nurse and hospital (A) 1062 mental 626 shortage of (P) 507, (P) 570 pulmonary tuberculosis in student (P) 54 recruitment of (P) 570, student (P) 570 training of (A) 804 (P) 814
Nursing—film on (Radzan) (C) 47 Light Through Clouds (film) 1281 mental (LA) 753 (C) 865 Principles and Practice of Surgical Nursing (Nash) (R) 1310
Nursing couple and instinct (Gunther) 575, (Jelliffe) (C) 1024
Nursing homes, private, charges made to hospitals by (P) 453
Nursing Times 1032
Nutrition—anæmia and (LA) 655, better (LA) 1061 malnourished community (Jelliffe) (C) 119 Nutrition Research Laboratories, Coonoor, report for 1953–54, 681
Nyrop J E, lung cancer (C) 253, (C) 872, (C) 1178

O

OBITUARY

Aspinall R S, 108—Avery, O T, 463, 571
Ballard J F 1132—Barber H W 207—Barry D T, 925—Bellwood K B, 977—Blacklock D B, 1332—Brown, C R 158—Brown, E V 571—Buckley, C W 1228—Burridge, W, 977
Carter F B, 413—Cassie, E, 1081—Casson E 53, 108
Davies-Colley, R 924—Deuchars, A. 108—Dixon P K 977
Everidge J 1280
Fleming Sir A, 621—Fothergill, C F 1080—Frew, R S 1229
Griffiths, C A, 1130
Hall G 210—Hamerton, A E 359 464—Hampshire, C H 310—Haslett, Sir W 55—Henshaw, L M E R, 413—*Hill H B 1029*—Hoodless D W, 1030—Horton R L, 359—Hutchinson, J R 1130
Keith Sir A 157
Ladkin, R G 728—Langdon Down R L, 1279—Lavelle, H A 1229—Lee, M B 209—Low, J B 413—Lowe J, 1080—Lukose, G M, 359—Lyster R A 1280, 1334
MacCallan A F 824—Macewen H A 1029—Malcolmson G E, 517—Marshall, C J 107—Martin Sir C 462 518—Mellanby Sir E 309, 359—Miller, J B, 259—Morland, E C, 974, 1030
Neil, J H, 311—Neuberger, M, 680
O Donovan W J 209
Perry, H M J, 727—Petrie G F 768 825
Rae H J, 1079—Rhodes C E, 1334—Roberts C G 260—Robson W M 1131—Rosenheim, O 1131—Rundle C, 463—Russ C 680
Salaman R N, 1333—Scotson F H, 728—Scott A C, 727—Solandt D Y 1130—Sprawson E C, 874
Treherne Sir F, 311—Turner, P 464
Von Anrep G 207
Wade, Sir H 516—Waller, H K 258—Webber H N, 107—Whillis, J, 312, 360—White J D 250—Willan R J 208—Woodside C J A 517

O'Brien, J R P, intrinsic factor, 847
Obscene Publications Bill (P) 670
Observer error *see* Radiology
Obstetrics—anæsthesia in (A) 956, Analgesie obstetricale (Jamain and Giraud) (R) 598 Antenatal and Postnatal Care (Browne and Browne) (R) 1006 Practical Obstetric Problems (Donald) (R) 952 psychiatry and (Hargreaves) 30 research in Aberdeen 1335
Occupational health service (Parker) (C) 255
Ochronosis ocular (A) 1162
O'Connor J antipyretics (C) 406
Ocular, *see* Eyes
O'Donovan W J (O) 209
Œdema, uræmic (Gough) 162
Œsophagus—œsophageal reflux (Creamer) 279, (Wells and Johnston) 937, and carminatives (Creamer) 590, X ray Atlas and Manual of Esophagus Stomach and Duodenum (Meuwissen) (R) 1157, *see also* Thrush œsophagitis
Œstrogens—in adrenogenital syndrome (Armstrong) 1051 Technique and Significance of Œstrogen Determinations *(Eckstein and Zuckerman)* (R) 1158
Ogawa T, and *Ogawa*, J, infantile diarrhœa (C) 671
Ogilvie Sir H, counting swabs (C) 770
Oil—diesel, dangers of, 1220, iodised reactions to (Green Armytage) (C) 105
Okos, G Raynaud's phenomenon (C) 52
Olbert T, cancer research (C) 1328
Oldfield M W C—congenitally short frenula of upper lip and tongue, 528, freeze-drying arteries, 888
Oldham, J B, laparotomy wounds (C) 819
Oleesky, S, myxœdema (C) 256
O'Meara, R A Q, medical education, 194
Omentum torsion of (Cooper) 130
O'Mullane, E J, chlorpromazine (C) 617
Onchocerciasis 681
O'Neill, D—epilepsy (C) 725 Modern Trends in Psychosomatic Medicine (R) 1006
O'Neill, J, pentolinium tartrate, 224
Onychodermal band (Terry) 179, (Steer) (C) 512
Operating theatre parallel beam portable spotlight for (Dawson Edwards) (NI) 849
Operation Rangoon Jail (MacKenzie) 520
Operations *see* Surgery
Operative, *see* Surgery
Ophthalmology, *see* Eyes
Oppenheimer, J R., speech by (LA) 87
Optic, *see* Eyes
Opticians, registration of (P) 571
Orbital *see* Eyes
Order of St John of Jerusalem 159
O Regan J B, tuberculosis (C) 152, (correction) 212
Origins and History of Consciousness (Neumann) (R) 1157
Orme E, My Fight against Osteo Arthritis (R) 902
Ormsby, O S, Diseases of Skin (R) 133
Orotracheal connection (Bullough) (NI) 236, 574
Orthodontic treatment (P) 967, for school children (P) 54
Orthohydroxybenzal isonicotinyl hydrazone (Bavin, Kay, and Seymour) (C) 303
Orthopædics *see* Surgery
Osborn, S B, circulation of uterine wall, 323
Osborne House 313
Osteo arthritis—deformans of Luschka joints (Cave Griffiths, and Whiteley) 176, (Crisp) (Henry) (C) 305 (Fisher) (C) 405, (Cooper) (C) 675, My Fight against Osteo Arthritis (Orme) (R) 902
Osteochondritis of hip, 1308
Osteoporosis 703 (Cooke) 877 929, post pregnancy (Nordin and Roper) 431, (correction 520) (Brailsford) (C) 513
Osteosclerosis *see* Bones
Ovaries—"ovarian" agenesis *see* Turner's syndrome virilism due to ovarian arrhenoblastoma (Evans and Jones) 436
Overhydration and underhydration (Davis) (C) 1077
Overlapping, need for (Parry) 609
Owen E N, teaching deaf children (C) 1330
Owen, J A, plasma proteins (C) 808
Oxdiazolones in tuberculosis (Brodhage) (C) 570
Oxford Regional Hospital Board, 261
Oxygen—estimation of in blood (Handforth) 1252, high pressure and radiotherapy of cancer (Churchill Davidson Sanger and Thomlinson) 1091
Oxygen cylinder carrier (Watson) (C) 822
Oxytetracycline, 56 therapy associated with thrombocytopenic purpura (Beckett and Foxell) 1053
Oxytocin continuous intravenous (Werblowsky) (C) 49 (Holmes) (C) 870

P

Pads pressure, for ulcerated legs 1335
Pædiatrics, *see* Babies Children
Page B H hair of pilonidal sinus (C) 873
Page I H, argentaffinoma (C) 198 (correction) 466
Pain—after trauma (A) 602, does reduced blood-supply cause? (Kelly) 747 headache (Jefferson) 60 of cancer (Jefferson) 59 relief of in incurable cancer (Maher) 18, (Maher) (C) 512, visceral (Jefferson) 60
Pain, K W E, instrument fo flexor retinaculum (NI) 654
Painless Childbirth (Lamaze) (film
Palate, soft, rash on (Todd) (C)
Pallis, C, spastic palsy (C) 868
Palmar, *see* Hand
Palmer, A W laboratory techn 154
Palsy, *see* Paralysis
Pancreas—islet-cell tumour of, hypoglycæmia (Grimson and Y pancreatitis (A) 1011
Papain treated red cells in detec incomplete antibodies *(Goldsmit*
Pappworth, M. H, Behçet's syndro 820
Para aminosalicylic acid, optic after administration of isoni (Sutton and Beattie) 650
Paralysis—(Carter) 908 cerebr cerebral centre for childr 1320 cerebral, research on Infantile Cerebral Palsy 1117, innocuous temporary (Rudolf) (C) 51, (C) 615, med associated with acute infection o (Bailey and Bolton Carter) 530, (C) 971, median nerve, follow stings (Birch) (C) 619; of lo surgery of 1307, paraplegia c retrospondylolisthesis (Roaf) 23 tic, and cerebral palsy in Scot 814 spastic paraplegia of mid (Marshall) 643, (Pallis) (C) 868
Paraplegia *see* Paralysis
Parathyroid glands—hyperparath and peptic ulcer (A) 341
Parfit, J growth in first five ye
Parfitt, D N, schizophrenia (C) 1
Parfitt, E M poliomyelitis 117
Parfitt, G J dental caries (C) 11
Parker W S, occupational health (C) 255
Parkinson, James (Morris) 761
Parkinson, Sir J, cardiology, 101
Parkinsonism—during treatment serpine (Stead and Wing) (C), gical treatment of (LA) 1109

PARLIAMENT

Aged 726, patients in Ed needs of, 814, sick, care of, Ageno, 53—Air pollution, radioactivity of, in London, *Aviation medicine textbook*
Babies newborn, identification —Birth-control in Colonies, Bodies bequests of 453—Br prisoners medical examination
Cadmium poisoning 453 50 punishment, 410—Child 350—Children and Young (Harmful Publications) Bill, Child s treatment in hospital, Christofi case 53, 302—Civil 453—Clean Air Bill 350— experiments at hospitals, 5 children 453 506—Comm medical man power 451— bequests of 453—Crash hel
Deaths from lung cancer, 96 treatment, priority, in Scotland, Dental work conservative land, 727—Dentists for sch dren 453, in Scotland 410, 917, recruitment of, 814—D morphine, 453—Diamorphine chloride ban on 965—Diet ents 302—Dispensing of eq preparations 506—Dissemin osis and war pensions 965—D telephones 768—Drugs cost of illicit traffic in, 350, prices of proprietary cost of, 302 in Scotland, 350
Flour extraction rates of, Fluoridation of water-supply, 412—Fluoride content of supplies 814—Food, increased diture on 917—Food poisoning, Foods, ' welfare 1022—Fo mouth disease 916
Gas poisoning, deaths from, General practitioners in N H S, *Group practice loans* 814
Hearing aids, 453, monopack, Heroin addiction to 13 on 965, 1271—Horror comics, 505—Hospitals beds for patients in 351 capital ment schemes of 507 clinical ments on children in 412 treatment and, 54 military, plans for new 410, shor pharmacists in, 412, use of Exchequer funds by, 412, hours of, 412
Industrial health, 54—Irradiation tection of workers from 505,
Leprosy in England and Wales, treatment of, in Colonies 768

l appointments in Colonies 506—
ical Research Council, allegation
nst refuted 768—Mental hos
l, medical superintendents of
—Mentally defective crimes of
—Mental nurses, shortage of
—Mercury in teething powders,
poisoning and pink disease
—Merit awards 600—Midwives,
ts of 351—Milk, heat treatment of
—Ministry of Food transfer of
tions of 767—Motoring offences
blood tests 967—Myxomatosis

al Health Service supplementary
mates 451—National Service re
ts medical standards of 412—
industrial Employment Bill, 814
uclear explosions defence against,
genetic effects of, 725-768—
nes recruitment of 570, student,
pulmonary tuberculosis among
training of 814—Nursing homes,
rate 453
ene *Publications Bill*, 679—
icians, registration of 571—
hodontic treatment, 967 for
dren 51
ysis spastic, and cerebral palsy
—Patients requests for lists of
—Pay of hospital doctors 506,
rmacists 966 — Pharmaceutical
orts, 571—Pharmacists at hos
ls, 814—Pneumoconiosis diag
s of 623—Poliomyelitis research
Scotland 13 5, vaccine 915
1022 1271 1325—Prescriptions,
, charges refunded 51—Prison
rm 1021 welfare officers 350—
chiatric social workers in Scotland
—Pulmonary tuberculosis among
dent nurses, 51
n s speech 1270
active substances 623—Radio
phy mass 51 units, mobile
—Raynaud s phenomenon, 413—
nploy Ltd financial loss on 917—
al Air Force civilian doctors in,
regular commissions, medical
ndard for, 623—*Royal Free Hos*
l Group inquiry 1271
l-children and milk tablets, 917—
ial services: 1020 and Budget
; future of, 1324 in Colonies
—Spastic children care of 452
ning of 302—*State scholarships*,
—Striker and doctor 1325
culosis eradication of bovine,
—Tuberculous British, treated
Swiss sanatoria 571 727
rsity grants 350
by post 1022

R. Examen clinique et traite
d un endocrinien (R) 952
, see Mumps
, H E. Sonne dysentery 16
, R H, overlapping 609
F C. foreign languages (C) 261
A., artificial respiration (C) 1330
D H.—cholangiography (C) 102
dal sinus (C) 772
—Color Atlas of Pathology
316 colour television in 314
ation of radiological and patho
l changes in some diseases of lungs
h) 161, *Histopathology of Respira*
Tract in Human Influenza (Hers)
791 in Army, century of (LA)
of rehabilitation (Fowler) 467
an) (C) 570
hrough Penguin City (Lillie) (R) 903
—aged almoners and (LA) 600
in Edinburgh, needs of (P) 814,
or emergency transport of patient
octor 8[illegible]6 chronic disposal of
ne and Warren) 1317 damages
Farman) (C) 48 diet of (P) 302,
r patient, and illness (Balint)
(Asher) 758, (Todd) (C) 810 pay
hospital beds for (P) 351, private,
for 1218 requests for lists of (P)
research and (Witts) 1115
herington) (C) 1180 *thought for*
, 1 08 unacceptable by doctors,
young long-stay in hospital
P) 1[illegible]63
D., aplastic anaemia 281
vaccinations (ML) 507; in
-health service 861 1321 leave
and (Smith) (C) 53 of chief
s *of L C C.* 36[illegible] of dentists
(I) 917; of hospital doctors (P)
of hospital pharmacists (P) 966
of house-officers 169 of sanitary
ctors, 571
T V femoral hernia (C) 101
Brown D A pituitary radon
nt, 1051
J. R Textbook of Gynaecology
) 1236

Peele T L Neuroanatomical Basis for Clinical Neurology (R) 1006
Pegum J S hydrocortisone ointment 1038
Pellagra and maize (Brande Kon Mitchell and Kodicek) 808
Pelvic congestion (A) 92
Penicillin fatal hypersensitivity to (ML) 912
Penman A C sanatoria (C) 509
Penman J vicarious appetite (C) 355
Pensions war and disseminated sclerosis (P) 905
Pentapyrrolidinium bitartrate *see* Pentolinium tartrate
Pentolinium tartrate—*heart failure from retention of salt and water caused by treatment with (Ronnov Jessen)* 13, *(Levene)* (C) 109 *initial control of* hypertension with (Ashby O Neill and Maclean) [illegible]1 (Evans) (C) 406
Pentosuria (Harris) (C) 7[illegible]0
Peptic ulcer—antacids for (LA) 1208 brain and (LA) 495 concomitant *gastric and duodenal ulcers (Johnson)* 300 (C) 775 duodenal causing hepatic abscess (Antin and Marker) 610 *duodenal perforated and sleeping* position (Elmhirst) (C) 721 gastric and cancer (A) 1161 hiatus hernia and *(Johnson)* [illegible]88, *hyperparathyroid*ism and (A) 311 in Southern Nigeria (Smith) (C) 50 (Rose) (C) 107 (Konstam) (C) 870 *primary of jejunum (Levitt and Saint)* 77 treated by gastrectomy in haemophiliac (Walker) 749 (Hardisty) (C) 817 *treatment of acutely perforated* (Moore) 163 (Grieve) (C) 308 (Moore) (C) 353 (Shepherd) (C) 408 (Kirkman) (C) 457 (Moore) *(Grieve)* (C) 507
Perambulator fumigated caused baby's death (ML) 912
Percival R.—*placenta praevia* (C) 867 (C) 972 placentography 1045
Periarteritis nodosa—associated with renal *tubular failure (Darmady Griffiths,* Spencer, Mattingly Stranak and de Wardener) 378
Pericardial, *see* Heart
Periodicals *see* Journals
Periodic syndrome (Wallis) (C) 1331
Peripheral Vascular Diseases (Allen, Barker and Hines) (R) 1310
Peritoneum—Maladies de l intestin et du péritoine (Rachet Busson and Debray) (R) 902 *see also* Pneumoperitoneum
Perkins, G Foundations of Surgery (R) 235
Perry H M J (O) 727
Personality *see* Psychology
Perspiration *see* Sweat
Perthes' disease—Legg-Calvé-Perthes Syndrome (Goff) (R) 353
Petch C P pulmonary hypertension (C) 460
Pethidine addiction to (ML) 97
Petrie G F (O) 768 825
Petty B W thrush oesophagitis, 991
Phaeochromocytoma and neurofibromatosis (Knox and Slessor) 790
Pharmaceutical Advisory Committee s report, 5[illegible]
Pharmaceutical *imports (P)* 571
Pharmaceutical services in hospitals 572
Pharmacists in hospitals—pay of (P) 966 1134 *shortage of (P)* 412 (P) 814
Pharmacology in Medicine (Drill) (R) 1107
Phear E A. blood-ammonium levels 836
Phenobarbitone *toxic effects of* (Scott) (C) 203
Phentolamine, adrenolytic effect of (Knox and Slessor) 790
Phenylbutazone as analgesic (Crowe) (C) 1016
Philip W M weighing machine (C) 153
Phillips D L Behçet s syndrome 366
Phillips, M. A fluoroacetate (C) 152
Phosphoethanolamine, urinary excretion of (McCance Morrison and Dent) 131
Phosphorus yellow *acute poisoning by* with recovery (Caley and Kellock) 539 (Todd) (C) 673
Photosynthesis *by isolated chloroplasts*, 159
Phthalyl sulphathiazole in Sonne dysentery (Abbott and Parry) 16
Physical and Psychical Research (Gregory and Kohsen) (R) 902
Physical medicine, department of 1116 (Mason) (C) 1227
Physical Signs in *Clinical Surgery (Bailey* and Clain) (R) 388
Physician and His Practice (Garland) (R) 1167
Physiology—Clinical Physiology of Lungs (Drinker) (R) 653 Physiology and *Biochemistry of Skin* (Rothman) (R) 133
Physiotherapy (A) 192
Physique and temperament (LA) 291
Pica (Muir) (C) 306
Pick, M I streptomycin (C) [illegible]3
Pickerill C. M. congenitally short frenula (C) 773

Pickerill, H P—angina (C) 151 congenitally short frenula (C) 773
Pickering G W appointment 835 875
Pictures in hospital wards (A) 140
Pierron J Diagnostic electrocardiographique (R) 1310
Pigmentation, *see* Pituitary gland
Pilonidal sinus hair of (Weale) 230 (Patey and Scarff) (C) 772 (Weale) (C) 8[illegible]1 (Page) (C) 873 (Brearley) (C) 9[illegible]3
Pink disease and mercury poisoning (P) 6[illegible]2
Piperazine derivatives and intestinal helminthiasis (Dunn) 592
Pirie, N W thermonuclear explosions (C) 918
Pitcher L tuberculosis (C) 1278
Pitt Rivers R. thyroxine analogues 285
Pituitary gland—Cushing's syndrome *radiotherapy of (Skrimshire)* [illegible]70; *hyper*pituitarism (Hubble) 1; hypophysectomy in diabetes (A) 1314, implanta*tion of radon seeds into (Forrest* and Peebles Brown) 1051, melanophore expanding activity of human (Hudson and *Bentley)* 380 *(Frazer)* (C) 513 (Hudson and Bentley) (C) 775 pigmentation and (A) 392 stimulation of *erythroblastic mitoses in bone marrow* by (Marinone and Corso) (C) 873 technique for demonstrating neurosecretory *material in human (Adams and Sloper)* 651
Placenta—praevia, radiography of (Russell and Warrick) 785 (Percival) (C) 867 (Hartley) (C) 9[illegible]1 (Percival) (C) 972 (Russell and Warrick) (C) 1074 soft tissue *placentography* (Percival and Murray) 1045
Plaster adhesive skin reactions with (Russell and Thorne) 67
Plaster-of paris reinforcement of (Thomas) (C) 205 (Pridie) (C) 407 with resin (Maudsley) 847
Platelets *see* Blood
Platt H muscular dystrophy (C) 719
Platt R cancer (C) 857
Pleural, *see* Lungs
Pleurisy tuberculous (A) 1162
Pleuropneumonia like organisms (Stokes) 276
Plug vaginal for procidentia (McCullagh) (NI) 491
Pneumoconiosis (Nagelschmidt) (C) 721 diagnosis of (P) 623
Pneumonectomy *see* Lungs
Pneumoperitoneum, artificial air-embolism in (ML) 729

POINTS OF VIEW —Holes knobs and wires (Turner) 763—*Institutional medicine* (Spence) 41

Poisoning by—aspirin, suppression of urine in (Miller) 596 barbiturate (Kellock) (C) 308 cadmium (P) 453, (P) 506, 1019 *carbon monoxide number of* deaths from (P) 623, extract of *Lippia rehmanni* (With) (C) 618 (Rimington) (C) 772, (With) (C) 1026 *iron (A) 532*, lead (Turner) 682 (LA) 754 (Browne) (C) 775 lead calcium disodium versenate *in (Giles Moore and Still)* 183 lead in battery cases (Gillet) 1118 manganese (Turner) 661 mercury (Turner) 661 pink disease and (P) 623; metals nervous system and (Turner) 661 methyl mercury (A) 35 sodium nitrite treated by exchange transfusion (Kirby) 594, yellow phosphorus (Caley and Kellock) 539 (Todd) (C) 673; *see also* Food poisoning Toxicology
Polani P E—chemical skin sex in Turner's syndrome 1[illegible]09 hypothermia (C) 773
Poliomyelitis—(A) 1010 crowds and (A) [illegible]43 *Diagnosis and Treatment of Acute* Phase of Poliomyelitis (Bower) (R) 1255 hypothermia in (Brohme) (C) 156 *(Rollason)* (C) 256 *(Haeger, Mörner* and Ryd) (C) 400 (Russell) (C) 457 (Haeger and Mörner) (C) 621, neonatorum (McMath) 631 (Cooke) (C) 921 outbreak in Barnsley 1323 quarantine in (Goffe and Parfitt) 1172 (Edwards) (C) 1[illegible]23 (Agerholm) (C) 1347 research in Scotland (P) 1325 Treatment of Acute Poliomyelitis (Spencer) (R) 235 vaccines (LA) 851 857 (I) 913 (A) 936 965, (I) 966 (Humble) (C) 972 1018, 1019 (P) 1022, (Russell) (C) 1071 1121 1175 (LA) 1202 1[illegible]20 1270 (P) 1271 (I) 12[illegible]5, virus, accidental inoculation with (McMath) 702
Polyarteritis nodosa *see* Periarteritis nodosa
Polyethylene effect of irradiation on 1323
Polyglot Medical Questionnaire (Parry) (C) [illegible]34
Polymenakos L G—syphilis (C) 822 word wanted (C) 306
Polymyxin 46
Pond A. G. viper wine (C) 156

Pond, D A, temporal lobectomy, 827
Populations—changes in, 864, local, estimates of for 1954, 351
Porphyrins (Vannotti) (R) 546
Postgraduate Medical School 1215
Postmaster General appointed, 806
Potassium—deficiency, tetany complicating treatment of, in renal acidosis (Fourman and McCance) 329 (Baar) (C) 459, plasma potassium levels in kwashiorkor (Holler and Schuleden) (C) 618, (Thompson) (C) 1181 radioactive, injected intravenously disposal of (Black Davies, and Emery) 1097 *see also* Uræmia
Potatoes, sprouting of prevented by irradiation 1323
Poulton, E M enuresis (C) 616
Practical Manual of Diseases of Chest (Davidson and Friend) (R) 236
Practical Obstetric Problems (Donald) (R) 952
Practice of Local Anæsthesia (Bankoff) (R) 134
Prankerd, T A J, myoglobinuria (C) 1072
Pratt, C A, shoes (C) 106
Precope, J, Medicine Magic and Mythology (R) 388
Prefrontal Leucotomy and Related Operations (Meyer and Beck) (R) 132
Pregnancy—Antenatal and Postnatal Care (Browne and Browne) (R) 1006 Gestation (Flexner) (R) 1108 iron deficiency anæmia in (Gatenby and Lillie) 740 osteoporosis after (Redman) (C) 971 (Nordin and Roper) 431, (correction) 520, (Brailsford) (C) 513 plasma level of 17 hydroxycorticosteroids in (Bayliss Browne Round, and Steinbeck) 62 toxæmia prolonged (Higgins) (C) 50, ætiology of (Sophian) (C) 404 *see also* Eclampsia, Placenta, Uterus
Preregistration year 1117 1221
Prerequisites of Good Teaching (Sachs) (R) 133
Prescribing economy in 1218
Prescriptions—dispensing of equivalent preparations (P) 506, number and cost of tetracycline, 681, refunds of (P) 412 of charges for (P) 54
Press and doctors 776
Pridie, K H plaster of paris (C) 407
Principles and Practice of Surgical Nursing (Nash) (R) 1310
Principles of Internal Medicine (Harrison) (R) 1006
Prison—reform (P) 1021 welfare officers (P) 350
Prisoners Broadmoor, medical examination of (P) 967
Pritchard E A B, disease of brain, 363
Pritchard E K sanatoria (C) 305
Private adventure money (A) 37
Prizes—Begley prize, 1082 Hallett prize, 627, Hancock prize, 415 Jacksonian prize, 927 John Hunter prize, 927, Juan Péron prize, 682
Proceedings of International Congress of Physical Medicine 752
Proceedings of World Conference of Doctors for Study of Present-day Living Conditions, 574
Procidentia uteri, vaginal plug for (McCullagh) (NI) 491
Proctitis, idiopathic granular (Cropper) 1253
Prostate gland—Retropubic Prostatectomy (Beneventi) (R) 1057, (correction) 1134, stilbœstrol phosphate and carcinoma of (Brandes and Bourne) 481
Prosthetics—Human Limbs and their Substitutes (Klopsteg and Wilson) (R) 752
Proteins—electrophoresis of serum proteins (A) 604, (Owen) (C) 868 (Consden) (C) 1015, (Miltényi) (C) 1181, (Christensen) (C) 1227 orthostatic proteinuria (A) 958 (A) 1163 proteinuria due to heart failure (Segall) (C) 1276
Province of Natal Centre, 1170
Pruritus treated with hydrocortisone ointment (Cochrane) (C) 568
Pseudocholinesterase control of axillary skin in Turner s syndrome (Polani and [illegible]) 1202
Psoriasis spondylitica (Fletcher and Rose) 695, (Lydon) (C) 918, (Buchan) (C) 1028
P S R scale (LA) 290
Psychiatrists' evidence in murder trials (A) 658
Psychiatry—children s psychiatric units in mental hospitals 28, chlorpromazine in (Vaughan, Leiberman and Cook) 1083, chlorpromazine in obsessive compulsive and allied disorders (Trethowan and Scott) 781 Clinical Psychiatry (Mayer Gross Slater, and [illegible]) (R) 83 depression treated with [illegible] (A) 1065 (Shottowe) (C) 1120, [illegible] (C) 1178 family, 858 Geistes [illegible] und Geistesstörung im Alter (Kielholz, Stoll, Vischer, Bühl, and Wyrsch) (R) 1058 lithium salts in manic psychosis (A) 854 Man Above Humanity (Bromberg) (R) 492 music in 519 obstetrics and (Hargreaves) 30, pioneers in (A) 393, (Walk) (C) 461 prophylactic, in children's homes (Neustatter) 807 (Thompson) (C) 919 psychiatric social workers in Scotland (P) 623 Psycho-chirurgie et fonctions mentales (Le Beau) (R) 1157, treatment of mental disease by sleep (Kerbikov) 744 *see also* Leucotomy
Psychology—Brain Mechanisms and Consciousness (Delafresnaye) (R) 800, cancer, psychological disease (Donaldson) 959, (Torrie) (Baker) (Grant) (C) 1075, (Donaldson) (Clapham and Solare) (C) 1177, (Boys) (C) 1124, Cardiac Symptoms in Neuroses (Baker) (R) 1206, doctor patient, and illness (Balint) 683 Emotions and Bodily Changes (Dunbar) (R) 850, Experimental Psychology (Woodworth and Schlosberg) (R) 1255, Fundamentals of Psychoanalytic Technique (Braatoy) (R) 336, Graphomotor Projection Technique (Kutash and Gehl) (R) 598, Meaning and Symbol (Digby) 926, neurosis, estimation of (Harris) 376 Origins and History of Consciousness (Neumann) (R) 1157 psychological aspects of uterine dysfunction (Ryle) (C) 46, (Tylden, Nixon and Ransom) (C) 404, (Reiss) (C) 456, (Cramond) (C) 566, psychological factors preventing rehabilitation (Fowler) 469 Psychometric Methods (Guildford) (R) 546, Tests in der klinischen Psychologie (Stern) (R) 1108 tuberculosis and personality (A) 855
Psychoses *see* Insanity
Psychosomatic diseases—in underdeveloped areas (Rose) (C) 1274, Modern Trends in Psychosomatic Medicine (O Neill) (R) 1006
Pteridines—Chemistry and Biology of Pteridines (Wolstenholme and Cameron) (R) 654
Public health—and mental health (LA) 135 (MacLennan and Small) 142, (Wilson) (Atkin) (Cameron) (C) 250, (Small) (Ring) (C) 405, (Harding) (C) 307, (Cameron) (C) 457, (MacQueen) (C) 565, (MacQueen) (C) 774, services in France (Cookson) 665
PUBLIC HEALTH—Alternative to health centres (Brooke) 98—Anthrax and bone meal fertiliser (Jamieson and Green) 560—Arsenic in food, 610—Cadmium poisoning 1019—Caravan sites 924—Child welfare centres, future of, 604—Cowpox in man (Laurance) 764—Dental care for mothers and children, 1269—Diphtheria notifications and deaths since 1945 561—Education of physically handicapped children 965—Fish and-chip shops, 146—Food, artificially coloured, 146—French public health services (Cookson) 665—General practices, geography of, 146—Health education, 247—Health of England and Wales in 1951 409—Housing (Brockington) 244—Hygiene in food establishments, 813—Influenza, 248 300, 610—Lead poisoning in Rotherham, 54, (Gillet) 1118—Local authority clinics, rôle of, 667—London control of health services of, 1175, in 1953, 93, water supply of, 863—Malignant disease of respiratory tract (Bradshaw) 861—Marriage statistics, 1121—Maternity and child welfare in Glasgow 206—Meningo-encephalitis lymphocytic, in Manchester (Tobin) 1267—Overlapping, need for (Parry) 609—Poliomyelitis outbreak 1323, quarantine in (Goffe and Parfitt) 1172 vaccine 965, 1018, 1019, 1121 1175 1270—Population changes, 864—Populations, estimates for local, in 1954 351—Puerperal pyrexia, notification of 147—Radioactive waste, uses of 1323—Salaries of doctors in public health service, 1221—School medical service 1069—Smallpox 147 206, 248, 351 410—Tuberculosis in Eire 1221, notification of 965 waiting lists in Scotland 206—Typhoid fever in Yorks, 351—Vaccination against Smallpox in London, 965— *see also* Infectious diseases Vital statistics
Puerperium—notification of puerperal pyrexia, 147
Pugh D L sanatoria (C) 614
Pullar Strecker H abundance and want (C) 1072
Pulmonary, *see* Lungs
Pulmonary stenosis, *see* Heart
Pulvertaft E L M, food in mental hospitals (C) 1278
Pump, blood transfusion (Lando
(Keating) (C) 154
Pundel, J P Diagnostic cyt
du cancer génital chez la
800
Punishment—capital (ML) 96,
(Hinden) (C) 465, corporal, of
children (Jackson) (C) 1027
(C) 1125
Pupils, *see* Eyes
Purpura—idiopathic throm
(LA) 494, 875, throm
associated with oxytetracycline
(Beckett and Foxell) 1053
Pygott, F, bronchography (C) 47
Pyloric, *see* Stomach
Pyrexia (Carter) 908, mechan
1114
Pyridostigmine bromide in m
gravis (Churchill-Davidson and
son) (C) 1123
Pyridyloxdiazolones in tuberculos
hage) (C) 570
Pyruvic acid, blood level of in h
in diabetes (Smith and Taylor)

Q

Quarterly Journal of Experimental
logy, 416

R

Rabies in Germany (A) 30, (Wells)
(Hemmes) (C) 821
Rabson, S M, protection of
(C) 819
Rachet, J, Maladies de l'intest
péritoine (R) 902
Rackow, F bronchography (C)
Radiation, *see* Irradiation
Radioactive—air in London (P
substances, use of (P) 623,
uses of, 1323, *see also* Isotopes,
Radiobiology *see* Irradiation
Radiography—angiocardiography
disease (A) 1315, arteriogr
Raynaud's disease (Lynn, Stol
Van Wyk) 471 (Barnett) (
bronchography (Pygott) (Rackow
mass (P) 54, of colon (A) 1
intestinal movements (LA) 189
(A) 1210, reducing observer
70 mm chest radiography ser
general practitioners (Stradl
Johnston) 1247, (LA) 1257,
(C) 1332, routine preopera
chest (Loder) 1150, units,
number of people examined by
xeroradiography (A) 957,
Cholangiography, Placenta
Radio isotope Conference, 1954 (J
(R) 545
Radiology—correlation of radiolo
pathological changes in some
of lungs (Gough) 161 De
Oral X Ray Diagnosis (Hu
(R) 800, Diagnostic Adv
Gastrointestinal Roentgenology
dick) (R) 1006, nomencla
1184, observer error in (Strad
Johnston) 1247, (LA) 1257,
(C) 1332, radiological diagnos
of perforation of peptic ulcer
103 radiological diagnosis of
of glomus jugulare (Hole
(Bickerstaff) (C) 255, Roentge
nostics (Schinz, Baensch, Fried
Uehlinger) (R) 186,
anatomische Grundlagen der
untersuchung (Kováts and Zeb
236, X ray Atlas and Ma
Esophagus, Stomach and D
(Meuwiesen) (R) 1157 *see also*
Radiotherapy—British Practice in
therapy (Carling, Windeyer,
Smithers) (R) 752, new linear
tor, 909, of cancer, high
oxygen and (Churchill Davidson
and Thomlinson) 1091, of C
syndrome (Skrimshire) 270
wave, of cancer, 573, with
Radium treatment of Hashimoto's
lymphomatosa and Riedel s thy
(Heggie) (C) 1127
Radon seeds implantation of
pituitary gland (Forrest and P
Brown) 1054
Radzan M, film on mental nursing
Rae, H J (O) 1070
Ragan, C, Connective Tissues (R)
Railway—accident at Sutton Co
298 (Cissane) (C) 562 (Scott) (
(Ross) (C) 865, striker and docto
(P) 1325
Ralli E P, Adrenal Cortex (R) 6
Ransom, S G, uterine dysfunc
404

see Russia
in (LA) 601
M. K artificial respiration

M recognition of tablets (C)

opropane, and dental extrac
rne and Morton) 20
in hospitals 448
J., institutional medicine 41
polyarteritis nodosa, 378
A. Treatment of Acute Polio
(R) 235
—Biochemistry of Semen
R) 84
ylosing spondylitis and leuk
nsworth) (C) 250 ; ankylosing
is treated with X rays incl
leukæmia in (Court Brown and
1283, cervical and nervous
LA) 18 cervical myelopathy
171 cervical spondylitis
tion in (Stamm) (C) 365,
(C) 459 osteoporosis of
931, retrospondylolisthesis
paraplegia (Roaf) 932 spinal
aged by Efocaine (Clarke
, and Roberts) 890 ; Spino
r Degenerations (Greenfield)
stress as factor in intervertebral
drome (A) 710 ; subacute com
generation of spinal cord with
stic anæmia due to spontane
olic fistula (Wilkinson) 74 ; see
o-arthritis, Scoliosis
gulation of (LA) 338 cortico
and splenectomy in acquired
ic anæmia (Barrie and Black
) 205 ; La rate et ses maladies
R) 540
ath, moulded direct to patient
) 841, (Walker) (C) 973
see Spine
thesis, see Spine
parallel beam portable (Dawson
) (NI) 849
E. death of 806, (O) 874
nt (Swerdlow) (NI) 1004
T, pattern of tongue 617
T., spondylitis (C) 365
A. R. rupture of duodenal
) 823
A) laparotomy wounds, 533

dvisory Committees 1117
., health education (C) 564
ci, infection by in newborn
with erythromycin (Forfar
Balf Wright and Gould) 584,
reen Hutchison and Neligan)
(Forfar Maccabe, Balf, Wright,
ld) (C) 1071, (Hay) (C) 1127,
reen Hutchison and Neligan)

of marriage in England and
1953 1121 *see also* Vital

parkinsonism during treat
h reserpine (C) 593
s, treatment of (Mann) (C)

sychodermal band (C) 512
gammaglobulinæmia (C) 1076
nedical care in S African town

A. W—adrenocortical secre
17 hydroxycorticosteroids

L. Raynaud's disease, 471
nsion Block (Moore) (R) 336
M. L blood-transfusion (C)

H L. cardiac *massage* (C)

n of—blankets with cetyl tri
nium bromide (Blowers and
1250 (Marsh) (C) 1331 food
yringes (A) 191 (Rollason) (C)
rmady and Hughes) (C) 513
hs) (C) 725 (Alexander and
) (C) 1228
Tests in der klinischen Psycho
1103
pression of (A) 140
w (A) 1112
P infant mortality 400
general practitioners holidays

K. Comet aircraft disasters

J, Geriatric Medicine (R)

l phosphate and prostatic car
(Brandes and Bourne) 481
ial poisoning 183
during cystoscopy (Mitchell)

J—Clinical Bacteriology (R)
europneumonia like organisms

A., Geisteskraft und Geistesstör
Alter (R) 1058

Stomach—achalasia of cardia in adolescents presenting with respiratory symptoms *(Davies and Roberts) 840* (Gibson) (C) 969 aftermath of gastric operations (A) 550 apparently homogeneous substance with intrinsic factor activity associated with cell particles from human (O'Brien Taylor Turnbull and Witts) 817 (Latner) (C) 921 Billroth I Gastric Resection (Moore and Harkins) (R) 30 ; Diagnostic Advances in Gastro intestinal Roentgenology (Bendick) (R) 1000 electrocardiographic changes after gastrectomy (Gardberg) (C) 512 electrogastrography (LA) 190 gastrectomy for peptic ulcer in hæmophiliac (Walker) 740, (Hardisty) (C) 817 gastrectomy rupture of duodenal stump after (Henson) 395 (Warren) (Schofield) (C) 721 (Lunn and Noon) (C) 823 (Nevo) (C) 870 (Stammers) (C) 923 gastrectomy total (LA) 937 (Richardson and Jennings) (C) 356 gastroscopy and chlorpromazine (Gill) (C) 301 (Douthwaite) (C) 354 (Gandara Maspule) (C) 612 leiomyoma of (Ker) 1306 leiomyosarcoma of (Horley) 1305 protective function of gastro intestinal tract against infection, 1004, pyloric antrum deformity of (A) 1112 *pyloric stenosis* and depletion of electrolytes (A) 90, (Andrejević) (C) 406 pyloric stenosis due to schistosomiasis (Rose) (C) 107, X ray Atlas and Manual of Esophagus Stomach and Duodenum (Meuwissen) (R) 1157 *see also* Peptic ulcer
Stones P B lymphocytic choriomeningitis 997
Story of Medicine (Walker) (R) 336
Stott, L. B 910
Strach E H cortisone corticotrophin and infection (C) 1197
Stradling P—chest radiography 1247 sanatoria (C) 402
Stranak F, polyarteritis nodosa 378
Stransky, E, jaundice (C) 1327
Strauss D H Sexual Disorders in Male (R) 186
Street L I was a Drug Addict (R) 1008
Streptococci—prophylaxis in streptococcal epidemics (A) 563 *Strep putridus* (A) 203
Streptomycin—*injections given to sleeping* children (Pick) (C) 53 in pulmonary sarcoidosis (Hoyle Dawson, and Mather) 938 oral, in Sonne dysentery (Abbott and Parry) 16
Stress in intervertebral-disc syndrome (A) 710
Stretcher of fibre-glass lined with foam rubber 209
Striker and doctor 1281 (P) 1325
Strom Olsen, R. leucotomy 986
Strong J A.—aplastic anæmia 281 glycyrrhetinic acid (C) 150
Stross B lung cancer (C) 63
Struma lymphomatosa *see* Thyroid gland
Strutt A., electric blankets (C) 1225
Stuart Harris C H Virus and Rickettsial Diseases (R) 1238
Studies on Fertility (Harrison) (R) 704
Sturdy D F diaphragmatic hernia 1001
Sue J M. shock (C) 1321
Sucrosuria (A) 906
Suction-cup for urinary fistula (Smith) (NI) 84
Suicide follow up of patients who had attempted (A) 141
Sulphadiazine resistance of meningococci to (A) 90
Sulphonamide sensitivity (Fox) (C) 203 (Lyell) (C) 251, (Marten) (C) 304
Sulphur and smoke (A) 919
Sulzberger M B Clinical Significance of Disturbances in Delivery of Sweat (R) 850
Summerskill, W H J blood-ammonium levels 836
Suprarenal glands—Adrenal Cortex (Ralli) *(R) 854, adrenalectomy for hypertension* (LA) 85 (Hanley) (C) 199 (d'Abreu) (C) 409 (Menof) (C) 620 adrenocortical secretion effect of adrenaline on (Hunter Bayliss and Steinbeck) 884 corticotrophin gel in test of cortical function of (Knox and Bradfield) (C) 433 failure of *glycyrrhetinic acid to control* insufficiency of (Strong and Wilson) (C) 150 Human Adrenal Cortex (Wolstenholme and Cameron) (R) 1108 in cholera (De Sengupta and Ganguli) 1013 prolonged stimulation of cortex of in rheumatoid arthritis (West and Newns) 578, *see also* Adrenogenital syndrome
Surgeries doctors—inspection of (ML) 1182 state of (ML) 1019
Surgery—Abdominal Operations (Maingot) (R) 1158, Atlas of Operations for Trauma (Russo) (R) 1037 ; Babcock's Principles and Practice of Surgery (Jones) (R) 387 British Surgical Practice Surgical Progress, 1954 (Carling and Ross) (R) 788 Foundations of Surgery (Perkins) (R) 235, Hey Groves Synopsis of Surgery (Wakeley) (R) 1157 in hæmophilia (Walker) 749, (Hardisty) (C) 817 *of paralysed lower limb* 1307 of pulmonary tuberculosis (A) 342 of temporal lobe epilepsy (LA) 903, operations on heart (Cort) (C) 153, (Wilson) (C) 201 Operative Orthopedic Clinics (Coron, Brockway and McMaster) (R) 1253 Physical Signs in Clinical Surgery *(Bailey and Clain)* (R) 388 reconstruction of hand digits (A) 1316 simplified operative routine for *carcinomatous* obstruction of colon (Brooke) 916 Surgery of Elbow (Smith) (R) 409 Surgery of Small and Large Intestine (Mayo) (R) 1108 Surgical Technigrams (Al Aki) (R) 288 surgical treatment of parkinsonism (LA) 1100 *see also* Arthroplasty, Laparotomy wounds Leucotomy
Susser M. medical care in S African township, 919
Sutton, I H optic atrophy 650
Sutton Coldfield railway accident 208 (Gissane) (C) 567 (Scott) (C) 621
Svensson, A., Crime Detection (R) 1056
Swabs counting (Riddell) (C) 669 (ML) 680 (Ogilvie) (C) 770
Sweat—(LA) 291 *Clinical Significance of* Disturbances in Delivery of Sweat (Sulzberger and Herrmann) (R) 850
Sweets and dental caries (Fielding) (C) 1339
Swerdlow M throat spray (NI) 1004
Switzerland—British tuberculous treated *in Swiss sanatoria (P) 571 (P) 727*
Sylvester J D writer's cramp 1147
Symonds H—enuresis (C) 455 (C) 676 medicine in Russia (C) 103
Symposia *see* CONFERENCES AND CONGRESSES
Symptoms functional in organic disease (Carter) 908 (McGlashan) (C) 972
Syncope *see* Fainting
Synkavit (Allison) (C) 669
Synopsis of Medicine (Tidy) (R) 134
Syphilis—serum tests for (Wilkinson) (C) 100 treatment of (Polymenakos) (C) 829 treponemal agglutination test (A) 1161
Syringes—sterilisation of (A) 191 (Rollason) (C) 408 *(Darmady and Hughes)* (C) 513, (Simbachs) (C) 725 (Alexander and Rollason) (C) 1228 unbreakable 519
Szabó R carditis (C) 678

T

Tablets—milk and school-children (P) 917 recognition of (A) 36 (Cooper) (C) 105 (Spalton) (C) 106
Tachycardia, *see* Heart
Talk, tact and treatment (Asher) 768
Taste simple method of testing (Mackenzie) 377
Tattersall W H sanatoria (C) 507
Tavares, A S sex of cancer and teratomata cells 948
Taylor A R, lumbar-plexus lesions, 988
Taylor I G, tuberculin testing (C) 19
Taylor K W pyruvic and *α ketoglutaric* acids 97
Taylor W H intrinsic factor 847
Teaching—of deaf children (Ingall) (C) 1226 (Owen) (C) 1330 of mental health 449, Prerequisites of Good Teaching (Sachs) (R) 133
Technique and *Significance* of Œstrogen Determinations (Eckstein and Zuckerman) (R) 1163
Techniques de réanimation médicale et de contrôle de l'équilibre humoral en médecine d'urgence (Hamburger Richet and Crosnier) (R) 288
Teeth—children's (Lime) *(C) 1274 ;* conservative dental work in Scotland (P) 727, Dental and Oral X Ray Diagnosis (Hutchinson) (R) 800 dental care for mothers and children 1269 dental extraction cyclopropane and sparks (Bourne and Morton) 20 dentures immediate *(A) 1316 ; extracted by* doctors 1230 films in dental emergencies 5 hospitals and dental treatment (I) 54 ; orthodontic treatment (I) 967 for school-children (P) 51 priority dental treatment in Scotland *(I) 614 ; see also* Caries
Teething powders mercury in (P) 571
Telephone and doctor (ML) 301 (I) 708
Television—colour in pathology 314 programmes medical (Welsh) (C) 1025 (C) 1126
Temperament and physique (LA) 991
Temperature—effective-temperature scales *(LA) 290 see also* Hypothermia
Tempest, M. N hydrocortisone (C) 569
Temple L. J sanatoria (C) 98
Tennis elbow (Crisp and Kendall) 466

Teratomata—mediastinal, sex of (Cruickshank) (O) 253, sex of cells of (Tavares) 918, teratomatous nævi (Weber) (C) 155
Terry, R B onychodermal band 179
Testes—deposition of iron in, after administration of iron-dextran (Nissim) 701, torsion of testis (Underhill) 129
Tests in der klinischen Psychologie (Stern) (R) 1108
Tetanus—fatal (ML) 680, nutrition and fluid and electrolyte balance during treatment of (Wilson and Care) 1303, treated with intravenous mephenesin (Docherty) 137, (Laurence) (C) 565
Tetany complicating treatment of potassium deficiency in renal acidosis (Fourman and McCance) 329, (Baar) (C) 450
Tetracycline—(McCorry and Weaver) 1102, in Sonne dysentery (Abbott and Parry) 16, in typhoid fever (Watson) 646 prescription of, 681
Tewfik, G I , chlorpromazine (C) 1179
Textbook of aviation medicine adopted for use of medical officers of Royal Air Force (P) 412
Textbook of Gynæcology (Peel) (R) 1256
Textbook of Gynæcology (Young) (R) 388
Textbook of Rheumatic Diseases (Copeman) (R) 752
Therapeutics—and philosophy (Beaven) (C) 200, Therapeutic Index (Miller and Ellenbogen) (R) 704 *see also* Treatment
Therapy, *see* Treatment

THE WIDDICOMBE FILE—βίος βραχύς 248—Clouded crystal ball, 811, (Hill) (C) 872—Hour of the angel, 1322—Mere 1-43—Merrygowhimbles, 1216—Noli episcopari 611

THE WIDER WORLD—Chinese medicine (James) 1068—Medical care in S African township (Susser Cormack, Stein and Hathorn) 912

Thibault, O , thyroxine analogues, 285
Thimann K V Vitamins and Hormones (R) 1005
Thiobarbiturate, new short acting (Nobes) 797
Thomas D F plaster of paris (C) 205
Thomlinson R H high pressure oxygen and radiotherapy of cancer, 1091
Thompson, J H , psychiatry in children's homes (C) 919
Thompson, M D , kwashiorkor (C) 1181
Thomson, A P , aortic aneurysm, 482
Thomson S appointment 1133
Thoracotomy *see* Lungs
Thorax, *see* Chest
Thorne, N A—hydrocortisone ointment, 1038 skin reactions beneath adhesive plasters, 67
Thornton J L Scientific Books Libraries and Collectors (R) 30
Three Men (Evans) 978
Throat spray (Swerdlow) (NI) 1004
Thrombocytopenia, *see* Blood
Thrombophlebitis following intravenous infusions (Morris) (C) 154, (Banerji) (C) 514
Thrombosis—cerebral, in young adults 1065 coronary and hoarseness (Scheuer Karpin) (C) 199
Through a City Archway (Chapman Huston and Cripps) 573
Thrower, W R , cowpox (C) 867
Thrush œsophagitis (Wolff, Petty, Astley, and Smellie) 991
Thwaites J G , Into General Practice (R) 186
Thymus and flavonoids (A) 443
Thyroid gland—carbimazole in thyrotoxicosis (Kirkeby and Romcke) 374, goitrogenic hazard of cobalt (James and Coles) (C) 50 Hashimoto's struma lymphomatosa (Cooke and Luxton) (C) 968 and Riedel's thyroiditis treated with radium (Heggie) (C) 1127 hypothyroidism (Hubble) 2, water diuresis in primary myxœdema (Oleesky) (C) 256 *see also* Basal metabolic rate Thyroxine
Thyrotoxicosis *see* Thyroid gland
Thyroxine, immediate effects of analogues of on biological oxidations in vitro (Thibault and Pitt Rivers) 285
Tidy, Sir H Synopsis of Medicine (R) 134
Till M myeloid leukæmia 425
Tobacco smoking—addiction to 1264, and pulmonary cancer (A) 392, (Mims) (Gould) (C) 1180 (Doll and Hill) (C) 1278
Tobin, J O H lymphocytic meningoencephalitis 1267
Tocopherol *see* Vitamin E
Todd A T—doctor patient and illness (C) 816 rash on soft palate (C) 49 yellow phosphorus poisoning (C) 673
Todd, R M isoniazid in primary pulmonary tuberculosis 794
Toes *see* Feet
Tomlinson B E , hepatitis, 1300
Tongue—congenitally short frenulum of (Oldfield) 528, (Pickerill and Pickerill) (C) 773, (Chapman) (Van Thal) (C) 871, pattern of human (Squires) 647
Tonsillectomy—inquiry into value of 1184 (Nash) (C) 1278 management of children undergoing (Gusterson) 940
Topley, E , blood loss in trauma, 629
Torrie, A , cancer (C) 1075
Torulosis, *see Cryptococcus neoformans*
Tough J S , lymphœdema præcox (C) 156
Toxicology—Handbook of Emergency Toxicology (Kaye) (R) 1005, *see also* Poisoning by
Toxoids, antigenicity of, and sympathomimetic drugs, 950
Toxoplasmosis, 652, myocardial (Cathie) (C) 149
Tracheobronchitis, postoperative membranous (Dark and Jewsbury) 430, (Colto and Flora) (C) 873
Trauma—assessment of blood loss in civilian (Clarke, Topley and Flear) 629, Atlas of Operations for Trauma (Russe) (R) 1057 endocrine response to, 1055, treatment of (A) 957
Treatment—abroad, currency for (Williams) (C) 103, by post (ML) 301, Diagnosis and Treatment of Acute Phase of Poliomyelitis (Bower) (R) 1255 Modern Treatment Yearbook 1955 (Wakeley) (R) 850, of injuries (A) 957, Reactions with Drug Therapy (Alexander) (R) 1005, talk, tact, and (Asher) 758 Treatment of Acute Poliomyelitis (Spencer) (R) 235
Tredgold R F leucotomy, 981
Treherne, Sir F (O) 311
Treponemal agglutination test (A) 1161
Tretamine (LA) 440
Trethowan W H , chlorpromazine 781
Trew, A., schizophrenia (C) 402
Trichloroethylene apparatus for midwives, 362
Trichocephalus dispar (Dunn) 592
Trigger finger (A) 551
'Triton A 20,' 'Triton W R 1339' in resuscitation of newborn (A) 601
Trocar and cannula, aspiration (Robson) (NI) 1309
Trolleys gas cylinder, British standard 1032
'Tromexan,' *see* Ethyl biscoumacetate
Tropics—Development of Tropical and Subtropical Countries (Banks) (R) 654
Troubled Mind (film) (Radzan) (C) 47
Troup, W A., heat to heart (C) 202
Trowell H C Kwashiorkor (R) 492
Trypsin, inhalation of, in bronchitis (Simpson) (C) 48
Tube—endobronchial (Gordon and Green) (NI) 185 endotracheal, harness for (Rolfe) (NI) 1256, fallopian, torsion of (Abbas) 128, pilot, for blood bottle (Campbell) (NI) 1058, *see also* Tubes
Tubercle bacilli isoniazid resistant (LA) 238 (Middlebrook and Dressler) (C) 669
Tuberculin—sensitivity in S African Bantu (Kuper) 996 testing, mass (Beddard) (Taylor) (Hargreaves) (C) 49, tests (A) 659 (Doig) (C) 823
Tuberculosis—bovine, eradication of (P) 412, carriage of tuberculous by air (A) 341, genito urinary (Ross, Gow and St Hill) 116 (Haines) (C) 203 (Gow) (C) 456, in children human source of (Briggs, Illingworth and Lorber) 263, (Cox) (Hall) (C) 407, in Eire, 1221 (Pitcher) (C) 1278, in immigrants (Macdonald) (C) 48, (Doig) (O Regan) (C) 152, (correction) 212, (James) (C) 251, (Hess and Macdonald) (C) 354 (Flynn and Joyce) (C) 461 (Doig) (C) 620, (James) (C) 771, (Macdonald and Hess) (C) 871, long term chemotherapy of (Joiner, Carroll Knox, and MacLean) (C) 49, notification of 965 of liver, atypical (A) 806 personality and (A) 855 pulmonary, apical localisation of (A) 89 (Wells) (C) 156, pulmonary chemotherapy and surgery in (A) 342, pulmonary dyspnœa due to chemotherapy of (Slade) 1203 pulmonary, in student nurses (P) 54 pulmonary lesions of (A) 1063 pulmonary primary in children (Walker) 218 pyridyl oxdiazolones in (Brodhage) (C) 570 sarcoidosis and, in a family (van Zwanenberg and Barry) 483 treatment of British tuberculous in Swiss sanatoria (P) 571 (P) 727 tuberculous lesions after chemotherapy (LA) 599 tuberculous lymphadenitis, peripheral, associated with visible primary focus natural history of (Miller and Cashman) 1286 tuberculous meningitis treated with cortisone (Ashby and Grant) 65, tuberculous pleural effusions (A) 36 tuberculous pleurisy (A) 1163 waiting lists in Scotland 206 *see also* Isoniazid
Tubes erythrocyte-sedimentat
standard, 211, *see also* Tube
Tuck, I M , torulosis 335, (C)
Tucker W E , cervical spc
450
Tully, R I J , Scientific Books,
and Collectors (R) 30
Tumours—arrhenoblastoma o
ing virilism (Evans and Ju
fibro adenosis and breast c
islot-cell tumour of panc
hypoglycæmia (Grimson and
leiomyoma of stomach
leiomyosarcoma of stomac
1305, neoplastic infiltrat
osteosclerosis (Weber) 386,
jugulare, diagnosis of (Ho
(Bickerstaff) (C) 255, orbital
phæchromocytoma and
sis (Knox and Slessor) 790,
Lymphoid Tissue (Lumb)
also Argentaffinoma Cancer,
Turkey sickle cell trait in
(Lohmann) (C) 672
Turkish army, medical mission
(Laws) 147
Turnbull A L , intrinsic factor
Turner, J W A , metallic p
Turner, P (O) 464
Turner Sir H , holes, knobs,
763
Turner's syndrome, pseud
content of axillary skin in
Magnus) 1202
Tuthill J F impotence, 124,
Tylden E , uterine dysfunction
Typhoid fever—in Yorkshire,
cycline in (Watson) 646
Tzipitl (Gómez) (C) 922

U

Ua Conchubhair S , antipyretic
Udenfriend, S , argentaffinoma
(correction) 466
Uehlinger E Roentgen Di
186
Ulcers—crural treated by
popliteal vein (Moore) 480,
(Anning) (R) 438, leg ulc
pads for, 1335 *see also* Po
Ultrasonic irradiation of frontal
38
Ulutin, O N , epilepsy (C) 677
Underhill, B M L , torsion of
Underwater sports, 769
UNICEF 1230
United Nations International
Emergency Fund 1230
United States of America, *see* U

UNIVERSITIES—Birmingham
ments 262 627 1081, d
fellowship, 627, finances, 414
pass lists, 57—Cambridge
313 415, 520, 627, 826 1
fellowship, 573—Dublin
diplomas, 826—Durham c
health, 1281 degrees 57—
chair of psychiatry 314, chai
health and social me
degrees and diplomas, 58, gu
research scholarships, 5
appointments 110 degrees,
Leeds chair of psych
degrees and diplomas, 776—
degree 776 Milne medal,
lists 57, 978 Warrington
978—London appointments,
681 927, chair of morbid
1183, chair of zoology 110,
110 415 681 927 diplo
fellowships, 627 pass lists
McGill chair of medicine, 628
psychiatry, 58—Manchester
826—Melbourne chair of
627 chair of surgery 627
University of Ireland de
New Zealand chair of obste
gynæcology, 58—Otago appo
1134—Oxford appointment
chair of medicine, 855, 875,
313 573, 1032 1281—St
pass lists 211—Saskatchewan
628, medical school, 628—
appointments, 58 465, 681, 11
at home to Sheffield town
chair of biochemistry, 681—
versity of Iowa appoint
Wales chair of bacteriology,

Universities grants to (P) 350
University College of West Indies 314
Uræmia—pulmonary œdema
(Gough) 162, uræmias (Bull)
Ureters transplantation of, in tub
(Ross Gow, and St Hill) 117
Urethritis (Lydon) (C) 918

bladder—cystoscopy diagram
(Badenoch) (C) 626 leg stirrups
opy (Mitchell) (NI) 848
d Morson bladder retractor (Lee)
335
fistula suction-cup for (Smith)
81
suppression of in aspirin poisoning
ter) 596
errors in (Davidson) (C) 120,
ght Americans 56 wrongful
of professor of medicine 128*
see Russia
bolism associated with rup
(Scrimgeour and Carrick) 435
(C) 615, (Birch) (C) 720 effective
of uterine wall in late preg
(Morris Osborn and Wright) 323
(C) 515 (Schuurmans) (C) 676
(C) 723 (Schuurmans) (C)
electrohysterography (A) 1210,
ale (A) 92; Hydergine a
on action of (Jeffcoate and Wilson)
(Bayly) (Jeffcoate and Wilson) (C)
psychological aspects of dysfunc
(Ryle) (C) 40 (Tylden, Nixon,
Ransom) (C) 404 (Reiss) (C) 456
nd) (C) 566; torsion of fallopian
(Ables) 128 vaginal plug for
ntia in elderly women (McCul
(NI) 401

V

—against smallpox in London,
see also B.C.G. vaccination
ons payment for (ML) 507
lymph and aureomycin (A) 498
(C) [illegible]
poliomyelitis (LA) 851 857 (P)
(A) 904 905, (P) 966 (Humble)
1016 1019 (P) 1022 (Russell)
1071, 1121, (LA) 1207 1230 1270
1271, (P) 13*5
(Laurance) 764
—inal plug for procidentia in
y women (McCullagh) (NI) 401
s due to new hæmophilus (A)
see also Behçet's syndrome
H endocardial fibrosis (C) 155
—for pulmonary stenosis (LA)
knife (Bentin) (NI) 134 (Sleeser)
11
J—hæmophilia (C) 869
cytopenia 593
A., Porphyrins (R) 546
J H., short frenula (C) 871
A. K., Raynaud's disease 471
berg D. sarcoidosis 483
virus, 544
see Blood-vessels
see Blood vessels
see Blood vessels
G L., chlorpromazine, 1083
K., lesions in ward 10, 663
radioactive sodium, 419
's syndrome (A) 710 ileu
popliteal vein for ulcers of leg
469; massive blood transfusion
cephalic vein (Dolton) 1052
vein stripper (Dodd) (NI) 1205
Thrombophlebitis
venereology and derma
(King and Russell) (C) 52
(C) 103, (Nicol) (C) 149
(C) 103, (Harrison) (C) 303,
and Russell) (C) 355 (Amsinder)
see Heart
(A) 1261
M.—hæmophilia (C) 869
thrombocytopenia, 593
epidemic with oculomotor com
(Lichtman) 2-8 (Bickford) (C)
(Kalmukers) (C) 467 (Burrows)
(Marshall) (C) 455 (Freedman)
(C) 614
appetite (Blair) (C) 300
(McGregor) (C) 335
Sir G., mental health, 521
J., mumps meningo-encephalitis,
J., cold baths (C) 516
(Rose) (Tread) (C) 156 (Sears)
(C) 204, (Nixon) (C) 252
due to ovarian arrhenoblastoma
and Jones) 136
idental inoculation with polio
virus (McIlrath) 782; Advances
Research (Smith and Lauffer)
1153
(LA) 339 direct floc
of influenza virus (Belyavin)
isolated from ablated tonsils (LA)
Virus and Rickettsial Diseases
Downie MacCallum and
Harris) (P) 1244 virus of yarl
and herpes zoster 541
L., Gesteskraft und Geistes
im Alter (R) 1044

Visual see Eyes
Vital statistics—births and deaths for third quarter of 1954 in Eire 147, births and deaths for third quarter of 1954 in England and Wales, 206, births and death for 1954 in England and Wales 248 813, births and deaths for first quarter of 1955 in England and Wales 965 births and deaths for 1954 in London, 147 births and deaths for 1953 in Northern Ireland 94 births and deaths for third quarter of 1954 in Scotland 54 births and deaths for 1954 in Scotland 813 health of England and Wales in 1954 409
Vitamin B_1 endogenous deficiency of (A) 91
Vitamin B_{12}, reaction to (Gillhespy) (C) 1076 (Bedford) (C) 1128
Vitamin C and infections (A) 443
Vitamin E in primary dysmenorrhœa (Butler and McKnight) 814
Vitamin K dangerous to newborn (Allison) (C) 669, (Moore and Sharman) (Laurance) (C) 819
Vitamins—Vitamins (Sebrell and Harris) (R) *35 (R) 387 Vitamins and Hormones (Harris, Marrian and Thimann) (R) 1005
Vomiting (Carter) 908 cyclical, 71 (Millichap) (C) 403 (Wallis) (C) 459 (Reimann) (C) 1*70
Von Anrep G (O) 20
Votes postal (P) 1033
Vulva see Behçet's syndrome

W

Wade Sir H death of 444 (O) 516
Waggoner R W mental changes and organic disease (C) 105
Wakefield E G Clinical Diagnosis (R) 1310
Wakeley Sir C—Hey Groves' Synopsis of Surgery (R) 1157 Modern Treatment Yearbook 1955 (R) 850
Walk, A pioneers in psychiatry (C) 161
Walker A R. P atherosclerosis (C) 605
Walker C H M—continuous murmurs, 272, primary pulmonary tuberculosis in children, 218
Walker D cortisone in injuries of hand (C) *02
Walker K.—Sexual Disorders in Male (R) 186 Story of Medicine (R) 330
Walker R A E plaster splints (C) 073
Walker W gastrectomy in hæmophiliac 749
Wallace E. R. sterilisation of blankets, 1250
Waller H K., death of 192 (O) 238
Wallis H R F—cyclical vomiting (C) 459 epilepsy 70 (C) 254 (C) 725; periodic syndrome (C) 1331
Wallman, I S. mumps meningo-encephalitis 1105
Walsh A., laparotomy wounds (C) 073
Walshe J M.—fœtor hepaticus 1230; hepatic coma, 1*35
Walshe Sir F Diseases of Nervous System (R) 1108
Walton A J laparotomy wounds (C) 973
War—blood transfusion of battle casualties (A) 241 civilian casualties in 159, pensions and disseminated sclerosis (P) 965 preparation for (Glaister) (C) 810 (Levy) (C) 923 see also Medical History of Second World War
Ward G, by any other name (C) 1332
Ward J hypersensitivity angiitis 1155
Warrack G H, *Clostridium welchii* 385
Warren, M W—chronic patients 1317; shared responsibility (C) 673
Warren, R. I ruptured duodenal stump (C) 721
Warrick C K placenta prævia 785 (C) 1074
Wasson, W W Auxiliary Heart (R) 653
Water—absorption of (A) 393; chlorination of 864 fluoride content of supplies of (P) 814; overhydration and underhydration (Davis) (C) 1077 supply of London 863 tracing underground flow of 863
Watson E H Growth and Development of Children (R) 492
Watson, H B oxygen-cylinder carrier (C) 822
Watson K. C. typhoid fever 616
Watson Williams E. J aortic aneurysm (C) 616
Wayne N D foreign languages (C) 6*
Weale F E., pilonidal sinus 220 (C) 821
Weaver J A., tetracycline 1102
Webber H N (O) 10
Webb-Johnson, Lord Christmas gifts (C) 151
Weber F P—osteosclerosis 35* teratomatous nævi (C) 155

Webster R. C M.D.O (O) 511
Weighing machine for patient in bed (Flear) (C) 101 (Phillip) (C) 153
Weiner W macroglobulinæmia (C) 100
Weissbach H argentaffinoma (C) 108 (correction) 166
Wellcome Historical Medical Museum 58
Wellisch H. Isaac and Œdipus (R) 438
Wellish, G C Syme's amputation (C) 102
Wells A L, tuberculosis (C) 150
Wells B G anæsthesia and heart (C) 921
Wells C hiatus hernia, 937
Wells O W, rabies (C) 674
Wells J W, Princess Louise Hospital (C) 367
Welsh, F, medical television programmes (C) 10*5
Welsh National School of Medicine 730
Weltraumstrahlung (Eugster) (R) 1*50
Wendel O Crime Detection (R) 1056
Werblowsky, R oxytocin (C) 49
Wertham F horror comics (C) 023
West H F, rheumatoid arthritis, 578
West Indies, appointments in (Arneaud) (C) 8*2
Wheat—diet gluten free results of late treatment with in cœliac disease (Gerrard Ross, and Smellie) 587 gluten and cœliac disease (Ross Fraser French Gerrard Sammons and Smellie) 1087
Whetnall, E, hearing-tests (C) 163
Whillis J (O) 312 360
Whitaker's Almanack 1955 (R) 336
White, J D (O) *59
Whitehouse M. W, Biochemistry of Aminosugars (R) 1057
Whiteley M. M. osteo-arthritis of Luschka joints 176
Whitfield A. G W malignant sensory neuropathy 233
Whittingham Sir H.—Comet aircraft disasters 1135 head injuries (C) 775
Whitwell, G P B Behçet's syndrome (C) 569
W.H.O see World Health Organisation
Wickenden P D barbiturate antagonist (C) 622
Wijesekera, N D J da S isoniazid (C) 407
Wilkinson A E. syphilis (C) 100
Wilkinson J F Modern Trends in Blood Diseases (R) 1107
Wilkinson M. C., sanatoria (C) 610
Wilkinson, R. W subacute combined degeneration of cord 74
Willan, R. J (O) 205
William Hyde Award 466
Williams, B L lymphocytic chorio meningitis 097
Williams C D kwashiorkor (C) 1071
Williams E. O eclampsia 1241
Williams H currency for treatment abroad (C) 103
Williamson D A. J hypothermi (C) 773
Willink Committee (P) 451 820
Wilmot A. J amœbic dysentery ( ) 1*23
Wilson, C tetanus 1303
Wilson C M. operations on ( ) et (C) *01
Wilson, J C—control of rats and mice (C) 201, mental health (C)
Wilson, J K Hydergin 1181 (C) 1329
Wilson J M. G glycyrrhetinic acid (C) 160
Wilson M. G rheumatic fever (C) 1123
Wilson I D, Human Limbs and their Substitutes (R) 763
Windeyer B W, British Practice Radiotherapy (R) [illegible]
Wing J K., parkinsonism [illegible] of with reserpine (C) 823
Wishart, M, acetazoleamide [illegible]
With T K liver poison (C) 1020
Witts L J—[illegible] research and patient 111[illegible]
Wolff O H., [illegible]
Wolstenholme G E. W [illegible] Biology of Pteridines (R) Adrenal Cortex (R) [illegible] Research (R) 30
Women see Gynæcol[illegible]
Woodside C J A. (C) [illegible]
Woodworth R S.—[illegible] logy (R) 1255
Wootton I D P.—[illegible] (C) 821
Words—made [illegible] wanted (C) [illegible]
Workshops for [illegible]
World Atlas of [illegible] waldt) (R) [illegible]
World Health [illegible] H.* H[illegible]
World Health [illegible] of ex[illegible]
World[illegible]
Wright[illegible] 591 [illegible]

Wright, H P, circulation of uterine wall, 323
Wright, J T, barbiturate antagonist (C) 1073, (C) 1329
Wright, S, chlorpromazine (C) 724
Writer's cramp, conditioning techniques in treatment of (Liversedge and Sylvester) 1147
Wylie, J C, Fertility from Town Wastes (R) 492
Wyrsch J, Geisteskraft und Geistesstörung im Alter (R) 1058

X

Xeroradiography (A) 957
X rays, *see* Radiography, Radiology, Radiotherapy

Y

Yell, J, islet-cell tumour of pancreas 334
Yendt, E R, hypophosphatasia, 286
Young, J, Textbook of Gynæcology (R) 388
Yudkin, J, lung cancer (C) 46, (C) 1025

Z

Zausmer, D M., mephenesin (C
Zelmanowits, J, cancer (C) 11
Zilkha, K J, compression of u
890
Zinneman, K S, freeze drying
888
Zoutendyk, A., agammaglobulin
1075
Zuckerman, S, Technique and S
of Œstrogen Determinations (

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